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The Role of Protein in Diets for Weight Reduction

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IN PRESCRIBING a diet for the reduction of obese patients one can choose between a low-calorie diet with an exceptionally high proportion of protein, or a diet with normal proportions of the various nutrients, but limited in total quantity. A century of clinical tradition[1] favors the first alternative. However, it might be proper at this time to re-examine the tradition.

Recent biochemical studies have revealed an unexpected metabolic activity of lipids in the fat stores; adipose tissue has been shown to have a significant complement of enzymes and synthetic capacities; various kinds of experimental obesities have been discovered and studied; new kinds of diets have been tested in metabolic experiments; the bulk composition of the human body has been estimated by indirect methods; the effects of starvation in wartime have been scrutinized in unprecedented detail. It would be surprising indeed if all this new evidence did not require some enlargement of our opinions.

Basic to much of the older thought on weight control was the assumption that the body could be divided into living protein material and dead storage matter.[2,3] It seemed evident that obesity, defined as an excess of inert fat added to an otherwise normal body,[1,4] should be treated with a diet that would eliminate the fat and preserve the "living tissue." Today, it is clear that the original conception of obesity was too simple. Fat tissue is neither inert, nor is it the only tissue that varies when weight is changed. It is not even certain that any reduction diet can transform an obese person into one with normal body composition and normal functional balance between the different tissues.

As a practical matter the main issues can be summed up in three questions: (1) Does a loss of nitrogen always cause damage to vital structures? (2) Is it desirable for an obese person to lose any nitrogen during weight reduction? (3) Does an exceptionally high proportion of protein in a low-calorie diet make the weight loss easier or faster? These will be taken up in order.

LOSS OF NITROGEN

Historically, numerous studies of nitrogen balance during underfeeding of both protein and calories were conducted in efforts to correlate metabolic rate and level of protein metabolism.[5] No damage to health was reported as incident to the nitrogen loss in the experiments. Benedict[6] and more recently Keys,[7] in comprehensive experiments conducted under close medical supervision, observed average total nitrogen losses of 175 and 430 g, respectively, roughly 24 and 27 g nitrogen/kg weight loss. Neither of these careful observers reported any dangerous symptoms associated with the nitrogen loss, or found any evidence in their follow-up studies suggesting a damage of vital structures.

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On the other hand, unbalanced high-calorie, low-protein, and vitamin-deficient diets can injure the liver, especially if they are fed to young, rapidly growing animals.[8–11] The abnormal mixtures used in these experiments have little counterpart in human nutrition, except for the high-carbohydrate, low-protein diets that cause the kwashiorkor syndrome in infants,[12] and the diets of some alcoholics who combine an excess of calories with a deficiency of protein and vitamins. These results are important in that they emphasize the need for a balanced proportion of nutrients in any diet, but certainly there is room to doubt whether experiments with harmful high-calorie diets have any relevance to the problem of weight reduction. All of the experimental studies agree in finding a high-calorie level essential for production of liver damage.[10] A careful search of the literature has failed to reveal *any* experiment in which liver disease or other nutritional lesion has followed simple restriction in the amount of a balanced diet (i.e., a food mixture with all nutrients in the relative proportions of a normal maintenance diet, fed in limited total quantity).

When both calories and protein were restricted in wartime diets, liver disease did not occur. Sherlock[13] employing biopsy and multiple liver function tests in a study of twenty-one malnourished German civilians, concluded that the apparent deficiency of lipotropic factors had failed to cause hepatic necrosis, cirrhosis or fatty change. Helwig-Larsen *et al.*[14] in an extensive study of starvation in German concentration camps, and of postwar rehabilitation, did not encounter acute liver failure or chronic liver damage. Epidemics of infectious hepatitis occurred in some camps, but appeared to run a normal course without unusual complications or subsequent cirrhosis. Extreme caloric deficit and wastage of muscular protein during imprisonment caused no structural damage that could be detected by ordinary clinical examination of 1,479 adult subjects after rehabilitation. Various studies of medical conditions in Japanese prison camps during the recent war showed no significant incidence of liver disease, although a considerable damage might have been expected from the unbalanced diets and the associated vitamin deficiencies.[15,16] Taking the prison camp medical literature as a whole, it is clear that the normal or the obese adult can adapt to caloric restriction and extreme loss of body nitrogen without suffering irreversible damage of vital tissues.

NITROGEN LOSS IN OBESITY

The desirability of any nitrogen loss is of course a separate question. The obese person has an obvious excess of carbon and hydrogen in his body. Does he also have an abnormal quantity of nitrogen? Can we, by diet, restore him to normal composition, and not merely to a statistically normal weight with abnormal proportions of lean and fatty masses? On these points the evidence is scanty and mainly indirect.

Simple overnutrition, produced by eating excess food, causes a much greater retention of nitrogen than can be attributed to the formation of adipose tissue with a nitrogen content of about 1.5 g/kg.[17] In experiments reported in the older literature, reviewed by von Noorden[18] and Grafe,[19] it was consistently found that overfeeding of calories produced massive retentions of nitrogen. The nitrogen to weight-gain ratios, calculated from the data in these reports, ranged from 16 to 28 g/kg. Two recent studies of overfeeding, one reporting nitrogen balance during two weeks of dietary excess,[20] and the other a densitometric measurement of body composition after six months of gain,[21] showed average values of the nitrogen to weight-gain ratio of about 18 and 7 g/kg, respectively. Adult animals, when fattened by liberal feeding and restriction of activity, retain nitrogen.[22] A popular theory attributes clinical obesity to simple overeating.[23] Since all available evidence indicates that the nitrogen retention during caloric overfeeding exceeds the amount in adipose tissue, no doubt advocates of this theory would agree that some nitrogen should be eliminated in treatment.

Keys[24] has provided more direct evidence that cellular material as well as fat is increased in human obesity. Estimations of "obesity tissue"—the excess matter found in the obese subject as compared with the normal, when body composition is determined by density or water content—showed 10 to 30 per cent cellu-

lar material, equivalent to 3 to 10 g of nitrogen/kg of excess weight If the goal of a reduction diet is the removal of obesity tissue, these figures indicate that at least 3 g of nitrogen/kg of weight loss should be eliminated.

In mice made obese by injection of gold thioglucose, the total nitrogen of the carcass has been reported as both normal[25] and increased.[26] Total nitrogen, however, measures essentially the muscle mass, and this in turn depends on the activity of the animal. Of more specific interest is the finding of a 50 per cent increase in liver mass in three different kinds of experimental obesity—gold thioglucose, genetic, hypothalamic.[25] Apparently there is a true hypertrophy of cellular material in the liver of the gold thioglucose-treated mice, since the dry, defatted weight of the organ was found to be increased.[27] The liver weight of obese human subjects apparently has not been studied in any systematic way, but the frequent abnormalities of liver function,[28] and the high correlation between excess body weight and deaths from hepatic or biliary disease[29] suggest that the liver may be involved in clinical obesity.

Studies of carcass composition after reduction of genetically obese mice[30] and after maintenance of hyperphagic rats in a reduced state by pair feeding with normals,[31] showed a decrease of total nitrogen and liver weight, and a relative excess of body fat. Evidently, the abnormal relation between cellular material and quantity of fat in these animals was determined by a metabolic disease rather than by the composition of their diet, since the obese mice and controls ate identical food mixtures. There appear to be no comparable studies of obese human subjects.

The obese patient tends to conserve nitrogen when the caloric intake is restricted.[32,33] The reason for this is obscure. It is difficult to see how a larger caloric surplus spares the nitrogen stores of obese people more efficiently than a normal amount of stored energy[34] protects people of average weight. Indeed, with respect to nitrogen balance the obese patient behaves more like an undernourished than an overnourished person.

Evaluating the limited evidence available, it appears that the obese patient combines a probable excess of nitrogen in his body with an abnormal tendency to conserve it during caloric starvation. The best treatment of obesity presumably would eliminate excess cellular material as well as excess fat, but only a tentative conclusion is possible at the present time. Evidently, much more work is needed to define body composition in the obese and reduced states, and to determine the sites of nitrogen accumulation and loss.

DIET THERAPY

The acceptability of a reduction diet often is interpreted in terms of a satiety value, which is a subjective term with variable meanings. As measured by actual consumption in unrestricted diets, protein foods obviously have a taste appeal, since the amount of meat and dairy products increases significantly when purchasing power rises above a marginal level.[35] However, the increase of protein is but part of a general caloric expansion; an analysis of the statistics shows a fairly constant proportion of protein calories over the whole range of dietary groups. Recent studies of food consumption in 32 countries[36] and in urban families of the United States[37] show that protein calories accounted for a strikingly constant fraction, 10 to 13 per cent, of total energy intake, despite wide differences in the kind of food eaten and a twofold range of calorie level.[38]

On starting a reduction diet, many patients find it hard to accept a restriction of protein foods;[39] but initial reactions are not necessarily a measure of long-term acceptability. With any diet the decisive test of its practical value is usage during a long course of steady weight loss. On this basis both high- and low-protein diets have demonstrated some value.

Strang, McClugage, and Evans, acting on the theory that a high proportion of protein would sustain the metabolic rate,[40] induced their patients to take about 60 g of protein per day in a 360 cal diet, thus furnishing about two-thirds of the calories as protein. As Evans pointed out,[41] "the menus make no concessions to gustatory sensualism," but in his clinic this diet was remarkably successful. Possibly it was near the upper limit of a practical high-protein diet. Rony,[42] discussing a diet with an

even greater proportion of protein, stated that "most obese patients refuse to follow it for any length of time." Mason,[43] on the other hand, reported satisfactory results with a reduction diet providing only 23 to 33 g protein per day. Our experience agrees with his. Patients treated with low-protein diets,[44] or with milk formulae providing 10 per cent of calories as protein,[45] have been willing to continue treatment for periods of several months. Some patients claimed that it was easier to follow one of these diets than the more traditional schemes, but a new plan always evokes some enthusiasm. The important point is that patients will accept a low-calorie diet containing only a normal proportion of protein, and stay with it long enough to lose a substantial amount of weight.

The theory that high-protein diets stimulate metabolic rate,[37] and thus accelerate weight loss, is not supported by actual tests. High-protein diets have been found to cause no faster losses of weight than isocaloric low-protein diets.[46,47] More specialized aspects of protein metabolism, stimulation of gastric juice[48] or rise of skin temperature in relation to dietary protein and calories,[49] have a physiologic interest but no obvious relevance to the practical design of a reduction diet.

As a proof of satiety in the objective sense of the word, protein added to an ample diet should reduce the total calorie intake when fat and carbohydrate calories remain freely available. This effect has been demonstrated in experimental animals only at very high levels of dietary protein; variations within the moderate range appear to have little or no influence on food intake.[50] Evans' diet,[41] containing such an abnormally high percentage of protein, may have depressed appetite in this way; other reduction diets with more moderate proportions of protein probably are not within the range for a significant effect on appetite. On the other hand, the results of one clinical study suggest that caloric appetite can be limited by reduction of protein intake. When dietary protein was limited to about 35 g/day, and other foods were available in surplus, the patients responded with a voluntary reduction of non-protein calories,[44] similar to the proportional limitation of calories and protein seen in diets of the poorer nations.[36] This is not to say that the subjects enjoyed the restriction of protein. All that was observed, or claimed by the authors, is that, subject to the restriction of protein, the patients chose to eat less non-protein calories. Apparently the obese patients, and the normal weight people in poor countries, elect a low-calorie diet in preference to one with an "abnormal" protein-calorie proportion.

So long as the metabolic causes of obesity remain unknown, the choice of a reduction diet must depend on practical experience rather than theory. The variety of temporarily successful treatments described during the past century make it obvious that the enthusiasm and gentle persistence of a physician,[51] the promotion of physical activity,[52] and control of general living habits count for much more in practical weight reduction than any chemical feature of the reduction diet.

SUMMARY

The published evidence indicates that obese patients can safely lose nitrogen during weight reduction. It suggests that some loss of nitrogen may be a proper part of reduction, since the obese subject probably has more than a normal amount of nitrogen in his body. Although in principle it is clear that the aim of a reduction diet should be a normal body composition, as well as a normal weight, there are no reported studies that relate the proportions of different reduction diets to changes in body composition. As an empirical measure for causing weight loss, a high-protein diet has no proven advantage over simple quantitative limitation of a diet containing a normal proportion of protein.

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Tocopherol Excess in Man

CREATINURIA ASSOCIATED WITH PROLONGED INGESTION

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AN ESSENTIAL role for vitamin E in human metabolism has yet to be established. However, its well documented indispensability to certain functions in experimental animals, and its seeming relationship to metabolic abnormalities described in patients apparently depleted of this substance suggest that vitamin E is probably also required by man.

Although tocopherol therapy generally fails to benefit patients with muscular dystrophy, the creatinuria that accompanies the reversible muscular disorders characteristic of vitamin E deficiency in other species may have a clinical counterpart. In a recently reported case of fatal biliary cirrhosis,[1] creatinuria and pentosuria were associated with an absence of measurable tocopherols in the blood serum, and were temporarily alleviated by tocopherol administration. Similarly, vitamin E therapy has inhibited creatinuria in infants with cystic fibrosis of the pancreas and biliary atresia.[2]

The present report describes an instance in which the experimental ingestion of an excess of tocopherol over a period of three months by an apparently normal subject was associated with a transitory creatinuria in the absence of other significant adverse clinical or laboratory effects.

CASE REPORT

A 41-year old physician ingested a total of 296 g of alpha tocopherol over a period of 93 days, in the following dosage: 2 g daily for 37 days; 4 g daily for 55 days; and 2 g on the final day. Two preparations were employed: Ephynal Acetate®† for the first 80 days; and Aquasol E®‡ for the last 13 days. Usually the vitamin was taken in two daily doses about eight hours apart, but there was no rigid adherence to this routine or to any fixed dietary regimen. There was no appreciable change in physical activity during the test period, nor were any significant intercurrent infections incurred.

RESULTS

The principal laboratory findings are indicated in the accompanying table and figure.

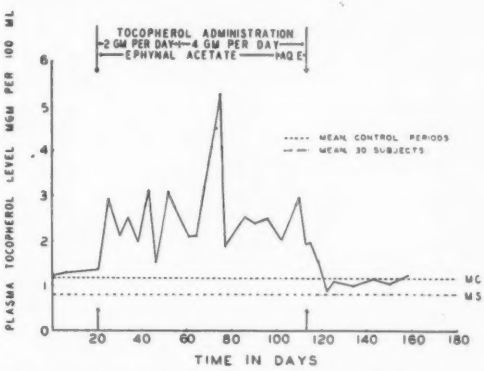

Fig. 1. Blood plasma tocopherol response to ingested vitamin E: 296 g DL-alpha tocopheryl acetate in 93 days.

The plasma tocopherol concentration, measured by a macro adaptation of the method of Quaife *et al.*,[3] showed a rapid initial rise followed by a variable plateau without overall increment, which was maintained throughout most of the test period at approximately twice

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† Ephynal Acetate, Roche, supplied in part through the courtesy of Dr. S. Evert Svenson, Hoffman-La Roche, Inc., Nutley, N. J.

‡ Aquasol E, U. S. Vitamin Corporation.

TABLE I

Plasma Tocopherol Concentration and 24-hour Urinary Excretion of Creatine and Creatinine Before, During, and Following Excess Tocopherol Ingestion

Observation day	Test period day	Plasma tocopherols*	Urine creatine†	Urine creatinine†
1	−19	1.26		
7	−13	1.39		
19	−1	—	0	1,704
20	1	1.41		
25	6	2.91		
29	10	2.25		
32	13	2.53		
36	17	2.01		
40	21	3.13		
43	24	1.53		
47	28	3.09		
60	41	2.18		
64	45	2.19		
68	49	5.39		
71	52	1.79		
83	64	2.51		
88	69	2.39		
92	73	2.41		
103	84	2.98	151.5	1,313
109	90	1.91		
110	91	—	143	1,324
111	92	1.94		
113	+1	1.53		
117	+5	0.81		
120	+8	1.10		
124	+12	—	0	1,322
130	+18	1.03		
139	+27	1.18	0	1,379
155	+43	1.03		
162	+50	1.24		
169	+57	0.76		
186	+74	1.29		
195	+83	1.29		
228	+116	1.40		

* Mg per 100 ml.

† Mg per 24 hours.

the usual concentration.* It returned rapidly to the pretest range when the tocopherol was discontinued. The mean fasting concentration of 2.26 ± 0.84 mg per 100 ml differed significantly (P less than 0.001) from the mean level of 1.15 ± 0.36 per 100 ml before and after the test period.† The fasting concentration was not appreciably higher on the daily dose of 4 than of 2 g, nor did the substitution of the aqueous dispersion for the nonwater-miscible preparation have any apparent added effect. Tocopherol could not be detected in the urine at times of maximum plasma concentration or over spans of several hours following ingestion of this substance.

A significant creatinuria was noted during the test period. On the day before initiation of the vitamin regimen, creatine was absent from a 24-hour specimen. On the 84th and 91st days of the experiment, the 24-hour excretion totals were 151.5 and 143 mg respectively. Twelve, and again, 27 days after the tocopherol was withheld, creatine could not be detected in 24-hour samples.

Creatinine excretion was questionably altered by the tocopherol ingestion. The output in the 24-hour period before the start of the test was greater by approximately 20 to 25 per cent than quantities measured on two occasions during, and two following, the experimental period. Except for a slight increase 27 days after the preparation was discontinued, these four readings were virtually identical. The excretion of 17-ketosteroids seemed unaffected by the tocopherol administration being 11.3 mg per 24 hours on the day before, and 11.9 mg on the 84th day of the tocopherol regimen. Blood cholesterol, carotene and vitamin A levels, the serum bilirubin level, cephalin flocculation, thymol turbidity, and the prothombin, bleeding and coagulation times showed no significant changes during the test period. The Harvard two-step test for physical fitness, Master two-step test, electrocardiogram and ballistocardiogram were likewise unaffected. Biopsy of the deltoid muscle at the end of the

* Repeated absorption tests showed considerable variation, with no consistent plasma response pattern. In general, following ingestion of amounts up to 4 g in a single dose, plasma tocopherol levels showed only small, gradual changes. Apart from the single fasting level of 5.39 mg per 100 ml, a concentration in excess of 4.0 mg per 100 ml was noted in only one instance, six hours after the ingestion of 4 g of tocopherol.

† The mean plasma level of 1.16 ± 0.39 mg per 100 ml before that period did not differ significantly from the level of 1.12 ± 0.20 mg per 100 ml following the experiment. However, the mean fasting level for this subject (62 readings before and after the test period) of 1.15 ± 0.37 mg differed significantly (P less than 0.0001) from the mean fasting level of 30 other subjects (72 readings) of 0.81 ± 0.26 mg.

experimental period revealed no deviation from the normal.

Clinically, no abnormalities were noted that could be attributed unequivocally to the large doses of tocopherol consumed. However, chapping cheilosis and angular stomatitis appeared early and persisted variably, but without progression, throughout the ingestion period. Gastrointestinal disturbances were frequent, especially during the final month, when abdominal distress and diarrhea with tenesmus were pronounced. Vague generalized muscle weakness and increased fatigability were experienced toward the end of the test period, but these wholly subjective complaints could not easily be evaluated. The untoward clinical manifestations disappeared within two weeks after the tocopherol was discontinued.

DISCUSSION

The average plasma concentration maintained in this case exceeded the usually accepted range of normal, but was lower than maximum levels reported with much smaller doses.[4–7] Higher levels have also been noted in the last trimester of pregnancy,[8,9] and in certain pathologic states without apparent excess ingestion of this substance.[9–11] The type of preparations employed may have been a limiting factor, and large amounts may have been lost in the stool.[5,12–14] Nevertheless, the lack of progressive increment in the blood, and, as in most other reported instances,[12,15,16] the absence of vitamin E from the urine, suggest that mechanisms other than those of absorption and elimination are involved in regulating plasma tocopherol concentration. Blood levels are temporarily depressed in a number of conditions not affecting intestinal fat transfer,[7,10,17,18] and so-called ceiling effects have also been noted by other observers.[2,13]

Creatinuria, as a phenomenon of tocopherol excess, is unexpected and not readily explained. Vitamin E reportedly influences pituitary-adrenal function and questionably affects the production of 17-ketosteroids.[19–22] Yet the unchanged steroid excretion in the present instance, although based on limited data, suggests that altered creatine metabolism does not result from modified adrenal or testicular activity.*

Tocopherol toxicity is readily produced in experimental animals. Although usually stated not to occur in man,[23] untoward symptoms have been reported on doses of 300 to 1,500 mg per day.[6,24–26] While a different dosage and/or different subject might have yielded higher plasma levels, with or without clinical toxicity, the absence of definite adverse changes in this case suggests an appreciable tolerance for tocopherol. Creatinuria, conceivably, may represent an early, subtle index of induced metabolic malfunction.

SUMMARY

Ingestion of 296 g of alpha tocopherol by a normal adult male over a period of 93 days resulted in a sustained average plasma tocopherol concentration of 2.26 ± 0.86 mg per 100 ml. This was statistically significant and approximately twice the control level of 1.15 ± 0.37 mg per 100 ml. A significant transitory creatinuria occurred during the test period, but there was no apparent change in the excretion of creatinine or of 17-ketosteroids.

There were no unequivocal signs of clinical toxicity. Exercise tolerance seemed unaffected. The electrocardiogram, ballistocardiogram, serum cholesterol, liver function and blood coagulation studies, and a muscle biopsy showed no deviation from the normal.

Creatinuria may be an early manifestation of an adverse metabolic effect induced by vitamin E excess.

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* This relationship is being investigated further. Preliminary observations suggest that a transitory creatinuria may, in some instances, be induced by a single large dose (4 g) of tocopherol, without prolonged ingestion of excessive amounts.

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A Formula for Estimating the Specific Gravity of the Human Body with a Consideration of Its Possible Uses

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KNOWLEDGE of the specific gravity of the human body is of interest for both physiologic and clinical reasons. An important use of it is in estimating the amount of fat in the body. Behnke[1] has theorized that the best basis of reference for basal metabolism is what he calls the *lean body mass* (LBM) by which is meant, essentially, the body without any stored depot or excess fat. He has suggested this as another way of expressing what Benedict and other older workers in energy metabolism called the *active protoplasmic mass*. This and related concepts have been reviewed by Keys and Brozek.[2]

Actual measurement of specific gravity of the human body *in vivo* is not a practical procedure for the average laboratory because it requires specialized equipment as well as specially trained personnel to operate it. Therefore, the development of any formula by which specific gravity may be estimated with reasonable precision should be of considerable practical significance. Obviously, proper use of any such expression requires that as much as possible be learned about its degree of precision and its limitations.

In 1927 Cowgill and Drabkin[3] published a formula for estimating the body surface area of the dog and discussed its implications as a basis for estimating basal metabolism not only for the dog but for other species as well. This formula differed from others already in the literature in that it contained an expression called the *nutritive correction factor*. A footnote to that paper mentioned the fact that human subjects differing widely in age show large differences in water content,[4] and therefore "it is possible that similar differences in specific gravity exist. This might account for the failure of surface area formulae based on weight alone and found satisfactory for adult organisms to hold for very young individuals." At the time that footnote was written such data on specific gravity as were available in the literature seemed to be very crude and unsatisfactory, and therefore suitable exploration of this point could not be made. More recently (1950) Hardy and Drabkin,[26] in their studies of the relation of body water to body size and fat content, reported that "an objective evaluation of overnutrition (excess fat) was derived from the nutritive index (Cowgill and Drabkin[3])." In the subjects studied here the total body water, evaluated as the D_2O dilution space varied between 73 and 43 per cent (inversely to "fat"). These investigators concluded that the "nutritive index" serves as an "excess fat index".

In 1942 Behnke, Feen and Welham[5] published the results of measurements of specific gravity made on members of the naval personnel. These data, interesting as they were for preliminary testing of ideas, were insufficient for our purpose because they were averages of data for groups rather than detailed data for each individual of the group. When this was

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brought to his attention, Captain Behnke kindly furnished all of his available data. For this I wish to express my deepest appreciation. This information was used for developing the equations reported in this paper.

The following items of information pertaining to 176 men in the U. S. Navy were supplied: age, height, body weight and specific gravity. In 62 of these same individuals basal metabolism was measured and given as calories per hour. This paper is a report of part of a study of these data, more particularly, a report of the discovery of a relationship between body specific gravity and a power function of height and weight from which several formulae for estimating specific gravity can be derived.

At the outset it was realized that this line of approach to the problem necessarily suffers from the important limitation imposed by the question "what is the meaning to be given the variable *weight* in such a formula?" One method of estimating body fat has involved attempts to arrive at an overall or average body density based on consideration of the densities of particular tissue systems and the proportion of the total body which these systems constitute.[6] Another method has involved attempts to compartmentalize the body with respect to total water, extracellular water, cell mass and fat.[7] It is quite evident that, like *in vivo* determination of specific gravity, these methods are not easily applied in clinical and physiologic work, certainly on any large scale. Therefore, if some formula could be devised that is sufficiently precise for most situations, and its proper limitations are ascertained, it should have considerable usefulness.

RELATION BETWEEN SPECIFIC GRAVITY AND A POWER FUNCTION OF HEIGHT AND WEIGHT

The Cowgill-Drabkin (1927) formula[3] for estimating body surface area of the dog contained what was called a *nutritive correction factor* (N_{max}/N_i). To determine it, the *nutritive index* of the individual in question (N_i) was first calculated. This index consisted of the ratio of the cube root of the weight to the body length ($W_g^{1/3}/L_{cm}$). The maximum value of this ratio for the species (N_{max}) would obviously pertain to the fattest possible individual; once calculated, it would serve as a constant in the nutritive correction factor. If the individual in question approximates the extreme of fatness, the value of this correction factor obviously approaches unity. The rest of the formula indicates that the surface area is proportional to a constant times the body weight raised to the 0.70 or 0.71 power. It is of some interest, and I believe significant, that the Galvao formula[8] for expressing the basal metabolism of fat men in the tropics is the same as this except for the value of the equating constant. Attention should also be called to the DuBois and DuBois[9] formula for estimating surface area in man. Here, the weight variable appears as $W^{0.425}$ and height as $H^{0.725}$. These and certain other observations which need not be gone into here suggested that a study of various relationships of powers of the weight to powers of the height might be worthwhile. Such a study was made using the data for 176 men studied by Behnke and associates. As a result, a relationship of the type $Y = aX + b$ was discovered, namely

$$\text{Specific Gravity} = 0.22\left[\frac{H_{cm}^{0.725}}{W_g^{0.5}}\right] + 0.75 \quad (I)$$

The deviations of the calculated values from those measured were as follows: standard deviation (S.D.*) = ±0.0131; standard error (S.E.†) = ±0.00099. Examination of the cases of "extreme" deviation, "extreme" being defined as "X times S.D.," gave the following results: with X = 1.5, 20 cases or 11.3 per cent; with X = 2, 7 cases or 4 per cent; with X = 2.5, 3 cases or 1.7 per cent; the maximum deviation was 2.7 times the standard deviation.

Examination of Equation I shows that its practical use would be made easier if either of the powers could be made equal to unity.

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* S.D. $= \sqrt{\frac{\Sigma\, \text{dev}^2}{n-1}}$.

† S.E. $= \sqrt{\frac{\text{S.D.}}{\sqrt{N}}}$ where N, degrees of freedom in this series = 175.

A study of this point led to the development of Equation II:

$$\text{Specific Gravity} = 0.8\left[\frac{H_{cm}^{0.242}}{W_{g}^{0.1}}\right] + 0.162 \quad \text{(II)}$$

In using Equation II, after looking up the logarithms of both height and weight, it is necessary to multiply only one of them by the exponent (that for height by 0.242); the proper log for the weight to use in the calculation is obtained merely by shifting the decimal point one place to the left.

The deviations of the calculated from the measured values using Equation II are almost identical with those for Equation I: S.D. = ±0.0130; S.E. = ±0.00097. "Extreme" deviations were: with X = 1.5, 21 cases or 11.9 per cent; with X = 2.0, 9 cases or 5.1 per cent; with X = 2.5, 1 case or 0.57 per cent; the maximum deviation was equal to 2.6 times the standard deviation.

Some workers may prefer to use an all-log form of Equation II. This proves to be:

$$\log \text{Specific Gravity} = 0.848\,(0.242 \log H_{cm} - \log 0.1\, W_{g} - 0.0172 \quad \text{(III)}$$

APPLICATION OF THE EQUATIONS TO INDIVIDUALS REPRESENTING EXTREMES OF HEIGHT AND WEIGHT

If these equations have validity, application of them to individuals representing extremes of height and weight should not give unreasonable or absurd results. In Table I are given the results of calculations of this type.

The individuals listed in Table I are described in chapter 7 of *Anomalies and Curiosities of Medicine* by Gould and Pyle.[10] In this chapter the weights of other persons are mentioned but without any information as to height. In some instances it seems evident that the weight was not measured with a high degree of accuracy. In such cases the weights actually given should be interpreted as "at least" figures. For example, Case 10 is reported as having weighed "17 stone." Since one stone is equal to 14 lb, this means that Case 10 weighed 238 lb. This could also mean "at least 238" but not more than another stone of 14 lb. On the other hand, consider Case 13, Daniel Lambert, "probably most famous of all fat men." His weight is reported as having been "52 stones, 11 lb." Here, evidently, an effort was made to weigh to the nearest pound. Considerations of this sort are mentioned in Table I.

In interpreting the specific gravity values given in column 4 of Table I, consideration must be given to what the upper and lower limits might be expected to be. The studies of Behnke and associates were carried out on healthy men. The highest value actually measured was 1.100. The following quotations from the Behnke *et al.* papers are very pertinent in this connection:

> "One may tentatively suppose that this value represents the overall density of a lean body mass (LBM) whose percentage composition is constant from individual to individual[1] . . . The value for the specific gravity of the LBM may actually be higher than 1.100. Values for the leanest person have never exceeded 1.100, but the presence of a 'minimal' amount of excess fat and possibly of intestinal gas in the subject at the time of the determination would tend to raise the specific gravity of the true LBM by several units. Furthermore, Rathbun and Pace[11] recorded a value for the eviscerated guinea pig of 1.096, corresponding to a fat content of 1.5 per cent. If the mineral content of the human body is about 50 per cent greater than that of the guinea pig, then a value of the order of 1.103 may be more nearly correct.[13]"

In the development of their formula by which the percentage of body fat may be calculated from the body's specific gravity, Rathbun and Pace[11] selected 1.100 as the upper limit, this to represent lean body mass with zero per cent of "fat." Their published Table covers the range of 1.100 to 1.002 for specific gravity and 0 to 49.3 per cent body fat. Values obtained by their formula are given in column 5 of Table I because of their interest in this discussion.

Theoretically, the lowest value for specific gravity of the body cannot possibly be below that of human body fat. What should be taken as this low limiting value? Behnke[1] used 0.93 for many of his calculations. Rathbun and Pace[11] used 0.918. Fidanza, Keys, and Anderson[13] studied the density of body fat in man and other mammals. On the basis of their report one can justify selection of 0.92 as the specific gravity at 37° C. With these theoretic upper and lower limits in mind, let us now consider the values yielded by our equations for the cases of "extreme" individuals listed in Table I.

TABLE I

Application of the Specific Gravity Formula to Individuals
Representing Extremes of Height and Weight

Case[1]	Height	Weight	Specific gravity [2]	Body fat [3]	Comments
	cm (ft in)	kg (lb)		percent	
					Abnormal leanness - "living skeleton" type
1	162.6 (5' 4")	27.22 (60)	1.150	-21.9	Edson, 1830: Could "chop a cord of wood without fatigue." Very high sp. gr.; excessive leanness.
2	137.2 (4' 6")	22.23 (49)	1.108	- 3.6	Salter's case, 1873; man, 32 years old. High sp. gr.: leanness but not of extreme type.
3	218.4 (7' 2")	74.85 (165)	1.121	- 9.8	"Leah the Giantess"-age 19 years. Photo in Gould and Pyle's book shows her very tall, extremely thin. sp. gr. indicates great leanness.
					Men of large frame - with and without obesity
4	269.2 (8'10")	181.9 (401)	1.085	6.8	1873, a young man "formerly in service of the king of the Netherlands." From description, was evidently just a "large man. sp. gr. agrees.
5	233.7 (7' 8")	138.8 (308)	1.079	9.6	Irishman, 1870: just "a big man". sp. gr. agrees.
6	268 (8' 9 1/2")	222.7 (491)	1.065	16.5	Robert Wadlow: acromegaly; died 1940, age 22 years. Has been called "tallest man in medical annals (?)" See case 4; also comment on case 8.
7	228.6 (7' 6")	163.3 (360)	1.059	20.0	"J. E.": acromegaly (Endocrinology 18:20, 1934). See cases 6 and 8.
8	218.4 (7' 2")	154.2 (340)	1.058	20.0	Brissaud & Meige case, 1895: "Male, 47 years of age, who presented nothing unusual before the age of 18, when he began to grow larger, until, having reached his majority, he measured 7 ft 2 in in height and weighed about 340 lb" sp. gr. value is on borderline between good nutrition and beginning obesity. For his height and age, might not be abnormal (Brozek & Keys, 1953). Was this acromegaly? See cases 6 & 7.
9	243.8 (8' 0")	226.8 (500)	1.042	28.1	"In 1712 in Holland there died a fisherman who was 8 ft tall and weighed 500 lb." These figures probably only approximate. sp. gr. suggests he was fat but not extremely so.
10	228.6 (7' 6")	205.0 (452)	1.039	29.7	Robert Hale, "Norfolk Giant" who died in 1843, age 43. sp. gr. indicates definite obesity.
11	219.7 (7' 2")	204.1 (450)	1.031	33.7	Captain Bates: "His body was well proportioned and his weight increased until it reached 450 lb;" sp. gr. for this weight indicates definite obesity.
12	160.0 (5' 3")	108.1 (238)	1.019	40.2	Case V in Wadd's famous book on obesity. Other cases are described but with height not given; sp. gr. indicated pronounced obesity.
13	193.0 (6' 4")	330.5 (728)	0.964	71.0	Wm. Campbell, landlord to Duke of Wellington: "not quite 22 years old when last measured." Cited as case of extreme obesity; sp. gr. agrees.
14	176.2 (5' 9")	279.7 (616)	0.960	73.4	Edward Bright, "fat man of Essex" (Lancet, 1827, 361); sp. gr. indicates extreme obesity.
15	180.3 (5'11")	335.2 (739)	0.950	79.6	Daniel Lambert, 1809, age 39: "probably most famous of all fat men." Weight recorded as "52 stone, 11 lb;" sp. gr. value only slightly above that for human fat by Behnke (0.93); Keys & Brozek give reasons why value could be 0.91. In either case, value for Lambert is still above theoretic limit; obviously represents extreme obesity, agreeing with the description of this case.
					Short stature. Dwarfs. Obesity in childhood.
16	55.9 (1'10")	16.33 (36)	0.978	62.8	Miss H. Woritz, American dwarf. Photo in Gould & Pyle's book shows a very fat face; sp. gr. means extreme obesity.
17	58.7 (1'11")	6.35 (14)	1.059	19.4	Princess Topaze, Paris, 1879. "...perfectly formed; vivacious;" sp. gr. indicates boderline between good nutrition and obesity.
18	124.5 (3' 3")	45.36 (100)	1.042	28.1	Isaac Butterfield, Leeds: "Weighed 100 lb, when two years old." If true, this must have been a case of extremely rapid growth early in life and not merely obesity; sp. gr. harmonizes with this. It indicates some obesity. This interpretation subject to greater error because in young growing individuals, the amount of extracellular water is greater; therefore proper interpretation of a value of 1.042 here presents some difficulties.
19	121.9 (4'0")	90.72 (200)	0.979	62.2	"Worcestershire girl" - 1788. Weight reported as "nearly 200 lb;" hence this calculation open to greater error and uncertainty. Cited as a case of obesity in childhood. Even allowing for some reduction in weight from 200 lb, the calculated sp. gr. is less than unity. Hence it is very probable that this was indeed a case of extreme obesity.
20	106.7 (3' 6")	92.08 (203)	0.952	78.4	Girl six years old; cited as case of obesity in childhood; sp. gr. agrees.
21	124.5 (4' 1")	139.7 (308)	0.948	80.7	Boy 13 years of age. Weight reported as "22 stone" (1 stone = 14 lb); hence an at least figure. Cited as case of obesity in childhood. sp. gr. agrees.
22	145.0 (4' 9")	79.38 (175)	1.023	37.9	Girl in Paris; 10 years old. Cited as case of obesity in childhood. sp. gr. definitely agrees.
23	167.6 (5' 6")	191.4 (422)	0.980	61.7	Millie Josephine, 13 years old. Photo in Gould & Pyle shows great obesity; sp. gr. agrees.

1. All of these cases except cases 6 and 7 are described in Gould and Pyle: Anomalies and Curiosities in Medicine, Chapter 7, pp. 324-364, W. B. Saunders, Philadelphia, 1900.

2. Calculated by the formula:

$$\text{specific gravity} = 0.8\ (Ht_{cm}^{0.242} / Wt_{g}^{0.1}) + 0.162.$$

3. Calculated by the Rathbun-Pace (1945) formula:

$$\text{Percentage of fat} = 100 \times (5.548/\text{specific gravity}) - 5.044.$$

Cases of Abnormal Leanness— "Living Skeleton" Type

The first three cases are examples of the "living skeleton" type, persons who are extremely thin. In each of these cases the formula yields a value greater than the 1.100 (or 1.103) mentioned as the theoretic upper limit. Several interpretations are possible.

(a) The assumption that 1.100 represents a human body devoid of "stored" or "excess" fat may not be quite correct (mentioned by Behnke—see above). The analysis of an emaciated human body by Widdowson, McCance and Spray[14] showing the presence of considerable "extractable fat" even after emaciation might at first thought be considered an argument in support of this view. This argument is weakened, however, by the difficulty we have here in properly defining "fat." In his analysis of the *lean body mass* Behnke[1] regards it as representing tissue having physiologically important lipid as part of its normal composition; such lipid would of course be extractable by ether or other organic solvents.

(b) Marked differences in body composition with respect to the heavier skeleton, softer tissues like muscle, skin, glands and others, could be responsible for values higher than 1.100. This would be expected certainly in individuals suffering or recovering from a wasting disease during which much of the soft tissue is lost. In this situation the relatively higher specific gravity of the skeleton would obviously play a more prominent part in determining the overall value for the entire body. In any formula of the type reported in this paper, marked reduction in the denominator of the fraction H/W would mean appreciable increase in the value of the fraction. This possibility requires further study to determine its validity and limitations.

(c) If the weight factor in this formula were to have extracellular water as an unusually large component, higher values for the estimation of specific gravity would be expected. "In prolonged undernutrition, the relative volume of extracellular fluid tends to become excessive."[15,16]

In the above discussion some of the points certainly apply to abnormal conditions such as wasting disease, prolonged undernutrition and the like. So far as can be determined, however, the first three cases of abnormally thin people in Table I were not suffering from such pathologic conditions. It is possible that sex differences may need consideration. Cases 1 and 2 were males, Case 3 a female. It does not appear possible at this time to do more than to mention these several possible lines of explanation. Detailed studies of body composition in such "extreme" individuals are obviously in order.

Cases of Extreme Obesity

In Table I several cases representing obesity of extreme degree are presented (see particularly cases 13, 14, 15, 19, 20, 21, and 23). For all of them the calculated values for specific gravity are well above the lower limit regardless of which of the three possible lower limits mentioned above is chosen.

Perhaps the most interesting of these to consider in greater detail is Case 15, the "famous fat man Daniel Lambert." If the Rathbun-Pace[11] formula is applied to the case* it appears that 79.6 per cent of Lambert's body weight of 335.2 kg (739 lb) was represented by fat. For his height of 180.3 cm and age of 39 years, his *standard weight* proves to be 78.5 kg. Therefore he was overweight by plus 366.7 per cent. Of this weight, 266.8 kg consisted of "fat" if we use the 79.6 per cent figure given us by the Rathbun-Pace formula. The difference, which might be called the "fat-free" body or LBM, amounts to 68.4 kg. Using this weight along with the height of 180.3 cm, our formula yields a specific gravity value of 1.086, which is certainly somewhere in the neighborhood of what would be considered "normal" for him, and what he should have been in light of prevailing concepts of "normality" with respect to leanness or fatness. Similar calculations can of course be made for the other cases listed in Table I, and they yield similar results. It is evident, then, that the calculated specific gravity values for all of the individuals who exhibited extreme obesity

* It is recognized that this represents an extrapolation—use that may or may not be justified.

TABLE II

Specific Gravity Values of the 51 Male Infants Ranging in Age from $2^1/_2$ hours to 7 days, whose Basal Metabolism was Measured by Benedict and Talbot (1914),[1] Calculated by the Formula:

$$\text{Specific Gravity} = 0.8\ (H_{cm}^{0.242}/W_g^{0.1}) + 0.162$$

Age	Number of cases	Specific gravity: Individual values[2]	Specific gravity: Average
$2^1/_2$ to 22 hr	23	1.094(2); 1.093(1); 1.088(1); 1.086(1); 1.085(1); 1.084(1); 1.083(2); 1.082(1); 1.079(2); 1.077(2); 1.076(3); 1.075(1); 1.072(1); 1.071(2).	1.080
1 to $2^1/_2$ days	10	1.094(1); 1.088(1); 1.085(1); 1.084(1); 1.082(1); 1.080(3); 1.077(2).	1.083
$2^1/_2$ to $3^1/_2$ days	8	1.090(1); 1.083(1); 1.080(1); 1.078(2); 1.065(1); 1.063(2).	1.075
4 to $4^1/_2$ days	7	1.105(1); 1.091(1); 1.089(1); 1.087(1); 1.081(2); 1.071(1).	1.086
5 to 7 days	3	1.098(1); 1.083(1); 1.077(1).	1.086
Grand average			1.081
Mean deviation			0.0037
Standard deviation (S.D.)[3]			±0.0079
Standard error of the mean (S.E.)[4]			±0.0013

1. Basic data for these calculations were taken from A on page 38 of *A Biometric Study of Basal Metabolism* by Harris and Benedict (1919).
2. Numbers within parentheses signify number of cases with this value.
3. $\text{S.D.} = \sqrt{\frac{\Sigma\ \text{dev.}^2}{n}}$.
4. $\text{S.E.} = \sqrt{\frac{\Sigma\ \text{dev.}^2}{n(n-1)}}$.

harmonize with acceptable theory and prevailing concepts.

APPLICATION OF THE EQUATIONS TO VARIOUS OTHER GROUPS OF DATA

Newborn Infants: Benedict and Talbot[17] studied the basal metabolism of 51 male infants ranging in age from two and one-half hours to seven days, the entire group being called "newborn infants." Because of the importance of body height or length for estimating surface area and its relation to basal metabolism, the lengths of these particular infants were measured with great care. Therefore, they constitute a good group with which to test the new equations. (The data actually used for this purpose were those given in Table A, page 38, of the monograph by Harris and Benedict.)[18] The results of our calculations are presented in Table II. The averages given in the last column are best understood by examination of the deviations for the various cases. Therefore they are summarized in the third column.

These individual values range from a high of 1.094 to a low of 1.063. If the Rathbun-Pace[11] formula for calculating body fat content from specific gravity is applied to these values, these extremes represent 3.2 and 17.5 per cent, respectively. The high values might have been expected in view of the long-known fact that the very young are characterized by having so much body water.[19] The low values, on the other hand, suggest the presence of an appreciable amount of body fat (17.5 per cent fat for the value 1.063). The chemical analyses of newly born mammals reported by Widdowson[20] and McCance and Widdowson[21] show that, whereas the newborn of the rat, mouse, cat, rabbit and pig contain from 1.1 to 2.1 per cent fat; that of the guinea pig contains about 10 per cent, and the human newborn contains about 16 per cent. Therefor the results of calculations presented in Table II are fully understandable and to be expected.

School Children: Numerous data on height and weight for growing children are available for study. No attempt was made at this stage of our investigation to examine such data in

TABLE III

Specific Gravity Values[1] for Various Age Groups of "Well-Fed" American School Children Compared with Those for "Protein-Deficient" Children in Jamaica, B. W. I. Calculations are Based on Mean Heights and Weights for Ages 4 to 18 Years

Age in years	"Well-fed" American School Children								"Protein-deficient children"
	Oakland-California		Davenport	Oak Park	California	Terman "gifted"	Iowa	Means (± S.D.[12])	Jamaica
	1892[2] (4956)[10]	1897[3] (4207)	1920[4] (563)	1922[5] (1398)	1923[6] (7463)	1923[7] (594)	1954[8] (12007)	for different years	1956[9] (1046)
4	---	---	---	---	---	---	---	---	1.099
5	---	---	---	---	---	---	---	---	1.106
6	---	---	---	---	---	---	1.093	---	1.104
7	1.085	1.090	1.099	1.095	1.094	1.092	1.095	1.093 ± .0041	1.103
8	1.091	1.093	1.100	1.095	1.093	1.099	1.095	1.095 ± .0031	1.104
9	1.090	1.092	1.098	1.095	1.094	1.090	1.092	1.093 ± .0027 [11]	1.102
10	1.091	1.091	1.104	1.094	1.091	1.092	1.094	1.094 ± .0043	1.101
11	1.091	1.091	1.098	1.093	1.092	1.090	1.091	1.092 ± .0025 [11]	1.102
12	1.091	1.090	1.098	1.093	1.091	1.091	1.090	1.092 ± .0026 [11]	1.101
13	1.084	1.091	1.098	1.090	1.090	1.090	1.087	1.090 ± .0040	1.098
14	1.086	1.086	---	1.086	1.088	1.088	1.086	1.087 ± .0010 [11]	1.092
15	1.086	1.085	---	1.088	1.086	1.087	1.084	1.086 ± .0013 [11]	1.094
16	---	---	---	---	---	---	1.080	---	---
17	---	---	---	---	---	---	1.083	---	---
18	---	---	---	---	---	---	1.079	---	---
Group Means:	1.089	1.090	1.099	1.092	1.091	1.091	1.088	---	1.101
S.D.[12]	±.0027	±.0025	±.0020	±.0031	±.0025	±.0032	±.0054	---	±.0040

1. Specific Gravity $= 0.8 \cdot (Ht_{cm}^{.242} / wt_{g}^{.1}) + 0.162$.

2. E. Barnes: Physical Development of Oakland Children. Oakland School Report, 1892-93, pages 38-44.

3. F. Boas: On the Growth of First-born Children. Science n.s., I: 402, 1895.

4. B. T. BALDWIN: In Genetic Studies of Genius, Vol. I by Terman et al., Stanford University Press, Chapter 7, Table 33, page 145. Baldwin wrote that "the Davenport group represents a selection from the best residential districts."

5. Baldwin wrote: "The Oak Park group is from the most favored section of Chicago."

6. H. K. Faber: Personal communication to B. T. Baldwin.

7. See footnote 4.

8. E. S. Eppright and V. D. Sidwell.[23] See Table III, page 552, data for boys.

9. Mackay et al.[24] See particularly Table II, data for boys, page 157.

10. Numbers within parentheses in column headings signify the number of children in the group.

11. The difference between this mean and that for the "protein-deficient" children (last column) is judged significant on the basis of the value of the critical ratio (difference between means being more than three times the standard error).

12. Standard deviation.

more than a preliminary fashion. An effort was made to find data pertaining to groups of children believed to be reasonably comparable with respect to economic status because of the bearing of low income on nutritional status. Baldwin's study of Terman's gifted children[22] was finally selected. The first six groups in Table III are those which Baldwin selected as being reasonably comparable with the Terman group. The seventh group[23] represents a much more recent study. All seven of these groups have been placed under a heading called "well-fed American school children" in order to contrast them with the "protein-deficient" children in Jamaica reported by Mackay and others.[24]

The specific gravity values for the "well-fed" children are pretty much the same, ranging from a high of 1.104 (fourth column, Baldwin's Davenport Study, 10th year) to a low of 1.084 (first column, Barnes Oakland Study, 13th year). Values such as these are characteristic of athletic young men. The Davenport children (fourth column) were evidently the thinnest of all the groups. The differences between the means for all the groups are not statistically significant. When the means for "years of age" (next to last column) are com-

TABLE IV

Specific Gravity Values for Groups of Boys with Abnormal Bodily Dimensions

(From Data by M. de Bruin[1])

Number of boys in group	Age	Height range from–to– cm	Weight range from–to– kg	Excess or shortage in height for age (first two groups) or Weight for height (last two groups) Range %	Average %	Specific gravity[2] Average (±S.D.[3]) (range)	Body fat content by Rathbun-Pace formula,[4] %
Tall Boys							
10	2.5–11.9	99–152	13.15–38	+7 to +16	+10.6	1.100(±.0021)) (1.112–1.088)	0 (−9.0(?) to +5.5)
Short Boys							
14	1.2½–12.7	77–136	6.30–30.8	−6 to −22	−11.6	1.082(±.0091) (1.097–1.064)	8.4 (1.3 to 17.0)
Abnormally Thin Boys							
6	2.0–15.2	93–166.5	12.7–42.65	−20 to −34	−23.5	1.108(±.0085) (1.120–1.095)	−3.7 (−42.1(?) to +2.3)
Fat Boys							
12	5.5–11.7	105–150	24.3–47.2	+20 to +56	+38.75	1.066(±.009) (1.080–1.048)	16.1 (+9.3 to +25.0)

1. de Bruin, M.: *Am. J. Dis. Child.*, 57: 29, 1939.
2. Specific Gravity = 0.8 ($Ht._{cm}^{0.242}/W_{g}^{0.1}$) + 0.162.
3. Standard deviation.
4. Rathbun, E. N., and Pace, N.: *J. Biol. Chem.*, 158: 667, 1945.

pared with the mean for the "protein-deficient" group (last column), the critical ratio* shows the differences to be significant for the 9th, 11th, 12th, 14th and 15th years.

For the "protein-deficient" children (last column) the higher specific gravity values for these ages signify definite leanness, absence of stored fat, and possibly greater amounts of extracellular fluid. Judged alone, such conclusions would not be justified; but when considered along with the other observations reported for these children, they are quite warranted. This illustrates how specific gravity values easily obtained by these equations might be used to advantage as either confirmatory or suggestive evidence to be considered along with other data.

* The Critical Ratio is defined here as the ratio of the difference between two means to the standard error of the difference between the means. Whenever the critical ratio is less than 2.0, the difference is considered statistically insignificant; when the critical ratio is between 2.0 and 2.9, the difference is of borderline significance; when it is 3.0 or higher, the difference is considered highly significant.

Boy Scouts: It is generally recognized that children tend to have more extracellular fluid than adults. On theoretic grounds one would expect this to be associated with higher specific gravity. This proves to be the case with the eight Boy Scouts who were the subjects of a study of basal metabolism reported by Harris and Benedict.[18] Five of the boys were 13 years old, four of them 14. Their mean heights and weights were 146 cm and 32.63 kg respectively. The specific gra· ity calculated by Equation I from these mean data proves to be 1.107 (±0.007). When the calculation is based on the heights and weights of each individual, the mean specific gravity (with S.D.) proves to be slightly higher, namely 1.110 (±0.007).

Boys with Abnormal Bodily Dimensions: M. De Bruin[25] has published data on the basal metabolism of children who were tall, or short, or abnormally thin, or fat. His Tables give height and weight data for each of the boys in his respective groups. Specific gravity values were therefore calculated for each in-

dividual. The results are summarized in Table IV. The values given in the last two columns agree very well with the group classification with some overlapping. For the "tall" and the "abnormally thin" boys the values for specific gravity are definitely high and the calculated values for body fat correspondingly low, with some overlapping for these two groups. On the other hand, for the "short" and the "fat" boys, the specific gravities are lower and the body fat values higher; here, too, there is some overlapping for the two groups. It is of some interest to mention that the highest specific gravity value (1.120) in Table IV (that for one of the "abnormally thin" boys) is identical with that for "Leah the Giantess" described in Table I (case 3).

Before and After Starvation: Since starvation involves loss of body weight, it is of interest to see what results would be obtained when these equations are applied to data for men before and after starvation. In developing their method for breaking down "body weight" into terms of extracellular fluid, cell mass and fat, McCance and Widdowson[7] studied two lean, five normal, and three obese men, as well as ten German soldiers repatriated from camps for prisoners of war in Russia. These soldiers were studied both before and after rehabilitation by suitable diet. In Table V are presented the calculated specific gravities for these individuals. Data on the per cent of body fat estimated by the Rathbun-Pace formula are also given. In column 4 are presented our interpretations of these specific gravity values reported in the third column. All of these values agree well with the judgments of the investigators themselves as to normality or obesity.

The specific gravity values under the heading "Before Rehabilitation" do not parallel perfectly the figures for "weight as per cent of standard," but they do agree in that with the exception of subject 10, the men were thin, some more so than others. Subjects 1, 4, 5, 6 and 8 may be classified as having had practically no body fat. According to these investigators the chief point of difference from the normal was an unusually large amount of extracellular fluid before rehabilitation. This agrees with what Keys and associates have reported.[15]

The values obtained "after rehabilitation" classify the men as "normal," that is, as having specific gravity values in the neighborhood

TABLE V

Specific Gravity Values for the Seven Normal and Three Obese Men, and Ten Repatriated German Prisoners Studied by McCance and Widdowson (1951)[1]

7 Normal and 3 obese men					10 German war prisoners repatriated from Russia							
					Before rehabilitation				After rehabilitation			
Subject	Weight as percent of standard	Specific Gravity [2]	Classification on basis of spec. grav.	Percent of body fat[3]	Subject no.	Weight as percent of standard	Specific Gravity [2]	Percent of body fat[3]	Weight as percent of standard	Specific gravity	Change in sp. gr. in rehabil.	Percent of body fat[3]
RM	77.7	1.108	lean	− 3.7	1	81.0	1.099	0.4	104	1.074	− .025	12.2
LH	86.0	1.096	lean	1.8	2	86.5	1.093	3.2	105	1.073	− .020	12.7
BS	90.0	1.087	"normal"	6.0	3	83.5	1.094	2.7	107	1.069	− .025	14.6
JR	94.0	1.088	"normal"	5.5	4	80.5	1.102	−1.0	100	1.080	− .022	9.3
AB	103.0	1.074	"normal"	12.2	5	84.0	1.102	−1.0	106	1.078	− .024	10.3
RD	107.0	1.074	"normal"	12.2								
JB	120.0	1.062	sl.obese	18.0	6	84.0	1.098	0.9	107	1.073	− .025	12.7
					7	85.5	1.095	2.3	104	1.075	− .020	11.7
G	184.0	1.028	obese	35.3	8	79.0	1.105	−2.3	105	1.076	− .029	11.2
N	193.0	1.017	obese	41.1	9	89.5	1.091	4.1	119	1.063	− .028	17.5
T	197.0	1.016	obese	41.7	10	91.0	1.088	5.5	113	1.067	− .021	17.6
					Mean	84.4	1.097	1.3	107	1.073	− .024	12.7
					Standard deviation	±3.6	±0.005		±5.1	±0.0049	±.003	±2.7

1. McCance R. M. and Widdowson, E. M.: Proc. Royal Soc. B. 138: 115, 1951.
2. Calculated by the formula: Specific Gravity = 0.8 ($H_{cm}^{0.242} / W_{g=}^{0.1}$) + 0.162.
3. Calculated by Rathbun-Pace (1945) formula: Percent Fat = 100 (5.548/sp.gr.) — 5.044.

of 1.073, which means about 12 per cent of body fat.[11] McCance and Widdowson in their paper express the opinion that "a person of standard weight for height contains 16 to 17 per cent of fat." Although the body weights of these men were quite "normal" for their heights after rehabilitation, the breakdown of these body weights into compartments showed that the men were still abnormal in bodily constitution. Evidently, then, proper interpretation of specific gravity values so easily obtained by these equations with data from patients in the clinic requires, among other things, that account be taken of any history of wasting disease or other condition associated with considerable loss of body tissue, and what is known about the effect of that condition on bodily composition. This study by McCance and Widdowson shows that restoration to "normal" bodily composition after great loss of tissue requires considerable time. A specific gravity value that could be taken as meaning body fat could really mean considerable water. This is one of the factors to be kept in mind when endeavoring to interpret specific gravity values properly.

SUMMARY

Using basic data on height and weight provided by Behnke and associates who measured the specific gravity in 176 normal men, three equations have been developed by which the specific gravity of men may be calculated from height and weight data. It is believed that these equations give results precise enough to prove useful in physiology and medicine.

These equations have been tested by being successfully applied to data in the literature for the following groups: (a) individuals representing extremes of height and weight ("walking skeleton" type and extreme obesity); (b) 51 newborn male infants; (c) seven groups of "well-fed" American school children; (d) a group of "protein-deficient" children in Jamaica; (e) a group of eight Boy Scouts; (f) four groups of boys classified respectively as tall, abnormally thin, short, and fat; (g) a group of seven normal and three obese men in whom studies of bodily composition were made; and (h) a group of ten German soldiers repatriated from camps for war prisoners in Russia, whose bodily composition was studied before and after rehabilitation by suitable diet. Considerations important for proper interpretation of such calculated specific gravity values are discussed.

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The Role of Nutritional Factors in the Cause, Prevention, and Cure of Alcoholism and Associated Infirmities

By ROBERT S. GOODHART, M.D.*

IN THIS discussion, I shall use the terms "alcoholism" and "alcoholic" simply for convenience in referring to the heavy consumer of alcoholic beverages. It is not to be inferred from this that I consider that a greater than average consumption of such beverages necessarily denotes addiction to alcohol.

That alcoholism may represent a manifestation of a metabolic defect, either congenital or acquired, that interferes with the normal utilization of certain customary nutrients is not a new concept. Recently, however, interest in this possibility has been reawakened by the work and writings of R. J. Williams who found that rats placed upon a marginal diet—marginal particularly with respect to the B vitamins—"drank heavily within a short period of time."[1] Rats on diets abundantly furnished with all the nutrients required by rats did not consume alcohol "beyond a low level." When animals that were drinking heavily on a marginal diet were supplied with an abundance of the missing nutrients, they often decreased their alcohol consumption to zero overnight and were maintained at this level as long as the required nutrients were supplied. That dietary deficiencies increase the voluntary consumption of alcohol by rats has also been reported by Brady and Westerfeld[2] and by Mardones *et al.*[3–6]

Williams found that different animals developed different deficiencies, all of which led to an increased consumption of alcohol. Why this should be has not been adequately explained, but, as Dr. Williams has stated,[1] a plausible explanation seems to be that rats on diets which do not furnish sufficient raw materials for the synthesis of various enzymes seek a source of easily derived calories. In any event, it seems clear that dietary deficiencies may lead to greatly increased alcohol consumption, at least in the rat.

Lowry, Sebrell, Daft, and Ashburn[7] found the development of polyneuropathy to be delayed in thiamine-deficient rats when alcohol was substituted isocalorically for part of the food intake. Similarly, Westerfeld and Doisy[8] found the isocaloric replacement of alcohol for fat or for carbohydrate in the thiamine-deficient ration of pigeons to delay the onset of opisthotonus and death. Butler and Sarett,[9] using human subjects, found the replacement of carbohydrate by alcohol in an adequate diet to result in an increased urinary excretion of thiamine and N_1-methylnicotinamide; indicating a sparing action of alcohol upon thiamine and niacin. A logical conclusion from these findings is that in all probability certain nutritional deficiencies, brought about primarily by inadequate diets, increased requirements, metabolic blocks, or a combination of these circumstances, in man may tend to increase the voluntary consumption of ethyl alcohol by man. But, this is a far cry from the postulation that alcoholism in man is basically a genetotrophic disease. If this be so, the fact has eluded me, although I have had years of experience with the treatment of alcoholics, both well nourished and malnourished. The recent study by Trul-

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son, Fleming, and Stare[10] sheds no light on this point, although it appears from their findings that many alcoholics may be benefited, in terms of reduced alcohol consumption, by multiple vitamin therapy. The effect of vitamin therapy in such instances, it seems to me, is more apt to be due to the correction of biochemical abnormalities and mental and somatic disorders resulting from vitamin deficiencies which, in turn, result from the poor diets and digestive disturbances associated with alcoholism, than it is to the correction of any original defect bearing a primary caustive relationship to the alcoholism. Alcoholics are a heterogeneous group and different people drink for different reasons. There is no alcoholic personality type.[11]

The chief pharmacologic effects of alcohol are well known and will not be discussed in this paper which is concerned only with chronic alcoholism.

In regard to the effects of chronic alcoholism upon the individual's mental and physical health, there is not one major disability found in association with this condition which does not occur, albeit less frequently, among total abstainers. The role of ethyl alcohol in the production of the complications of alcoholism, wherever it has been adequately investigated, has been shown to be that of a conditioning rather than a primary or precipitating cause. Let us examine, briefly, some of these complications.

Delirium Tremens: Delirium tremens not only occurs in chronic alcoholism but also frequently follows injuries, operations, and acute infections.[12–14] The primary defect is dehydration and salt depletion. Treatment consists of forcing fluids, administering sodium chloride, and providing an adequate calorie, high vitamin intake. Sedation is used sparingly and restraints no more than absolutely necessary. Flink *et al.*[15] found low serum magnesium concentrations in both alcoholic and nonalcoholic patients with delirium tremens and reported on the effective use of magnesium sulfate in the treatment of this condition.

Wernicke's Syndrome: Wernicke's syndrome is characterized by clouding of consciousness, varying ophthalmoplegias, and ataxia. Peripheral polyneuropathy is almost invariably present. As a matter of fact, I have never seen a patient with Wernicke's syndrome who did not also have a peripheral polyneuropathy. Wernicke's first case was a 20-year old woman who was not an alcoholic.

In 1940, Goodhart and Sinclair[16] reported zero blood levels of thiamine in a subject with Wernicke's syndrome. In 1941, Jolliffe, Wortis, and Fein[17] reported their conclusions from the discriminate therapy of 27 cases; to the effect that the ophthalmoplegia is a thiamine deficiency and that the other manifestations of the syndrome described by Wernicke are the results of other nutritional deficiencies or metabolic blocks. Their findings were confirmed in a 1952 report by Phillips, Victor, Adams, and Davidson.[18] These authors concluded "that the ophthalmoplegia of Wernicke's syndrome is related to a specific lack of thiamine. The nystagmus and ataxia also appear to be related to thiamine deficiency, but the evidence is less conclusive. No definite conclusions can be drawn regarding the relationship of the mental disturbances to the deprivation of thiamine or other vitamins." Obviously much remains to be clarified about the etiology of the complete syndrome described by Wernicke; however, since the syndrome occurs, in its entirety, in numerous conditions other than alcoholism, it is equally obvious that alcoholism can not be the immediate cause.

Alcoholic Encephalopathy: This syndrome is characterized by clouding of consciousness, changing cogwheel rigidities, and uncontrollable sucking and grasping reflexes. It has been repeatedly observed in nonalcoholic pellagrins.

Jolliffe[19,20] reduced the expected morality in alcoholics with this condition from 89.4 per cent to 12.5 per cent by treatment with niacin. He suggested that the syndrome should be termed "niacin deficiency encephalopathy," since niacin deficiency, not alcohol consumption, *per se*, is the cause.

Korsakoff Psychosis: As pointed out by Jellinek and Jolliffe,[21] the findings of all investigators point to much greater therapeutic success in the treatment of Korsakoff psychosis when the B vitamins are administered than

when they are not given. The improvement involves both the neurologic aspects and the mental symptoms. Bowman, Goodhart, and Jolliffe[22] have called attention to the high incidence of polyneuropathy in patients with Korsakoff psychosis in alcoholism, pregnancy, hyperthyroidism, and diabetes mellitus, which, in these cases, responds to thiamine therapy. These workers reported a threefold greater rate of recovery in patients treated with a good diet plus 10 to 50 mg of crystalline thiamine daily, by injection, than obtained with a good diet alone. They did not indicate their findings were conclusive, but recommended further studies of the relation of nutritional factors to the cause and treatment of Korsakoff psychosis, with greater numbers of patients.

Peripheral Polyneuropathy: There can be no doubt but that the polyneuropathy of the alcoholic is due to a nutritional deficiency and that, if adequate treatment is instituted before irreversible anatomic changes occur, it responds to nutrient therapy. In the great majority of such cases, thiamine deficiency is the primary etiologic factor;[23-26] however, other nutritional deficiencies also have adverse effects on the peripheral nerves. Recently, Bean, Franklin, and Sahs[27] have reported prompt improvement in nutritional peripheral neuropathy after intramuscular injection of vitamin B_{12}. Good results with the use of large doses of vitamin B_{12} have been reported by Lereboullett and Pluvinage[28] and by Menof.[29,30] Fernández[31] has employed vitamin B_6 in certain cases with good results. This simply serves to emphasize the fact that vitamin deficiencies in man generally are multiple, and that the various systems of the body are susceptible to deficiencies of not just one but of a number of nutrients.

Toxic Amblyopia: Carroll[32] divided 25 patients with tobacco-alcohol amblyopia into four groups; one group received an adequate diet supplemented with brewer's yeast; the second group received the usual hospital diet supplemented with entire vitamin B complex; the third received a definitely inadequate diet supplemented with large amounts of the vitamin B complex, and the fourth group received the same inadequate diet supplemented only with crystalline thiamine. All patients continued their customary use of alcohol and/or tobacco. All patients improved, the results being at least as good, according to Carroll, as any that he had previously obtained, even in patients who abstained from the use of tobacco and alcohol while under treatment.

A similar amblyopia has been observed in malnourished American soldiers released from Japanese prisoner-of-war camps and among malnourished children on the island of Jamaica.[33] The name "nutritional retrobulbar neuritis" has been given to this condition.

Fatty and Cirrhotic Livers: Fatty livers and cirrhosis of the liver occur in many conditions other than alcoholism. Of 129 alcoholics with fatty livers, Texon[34] found 90 per cent to have been on inadequate diets. All but one of 17 patients with cirrhosis of the liver had deficient diets, according to Texon. In the experimental animal, Best *et al.*[35] found that there is no more evidence that there is a toxic effect of pure alcohol on the liver cells than there is of a poisonous action of an equicaloric amount of sugar. They also found that the pathologic changes produced in the liver, by diets containing large amounts of alcohol or sugar, could be prevented by adequate amounts of choline, methionine, or casein. They attributed the pathologic changes found in the liver to an imbalance of calories and vitamins, particularly to a deficiency of lipotropic factors consequent to an increased caloric intake. While fully confirming Best's finding that adequate amounts of choline or methionine abolished the adverse effects on the liver of both alcohol and sugar supplements, Klatskin and his associates[36,37] found alcohol actually to have a specific effect in increasing the choline requirement, independent of the caloric intake.

In human subjects, Zieve and Hill[38] found no demonstrable relation between impairment of hepatic function and increasing degrees of alcohol consumption. Numerous studies on man indicate the importance of an adequate diet, ample in content of protein and lipotropic factors, in the treatment of the individual with a fatty or cirrhotic liver.[39-42] Phillips, Gabuzda, and Davidson,[42] conclude that their results in the treatment of fatty and cirrhotic livers in man "suggest that the improvement observed

was related to the provision of an adequate diet and that a subsidiary, if any, role was played by withdrawal of alcohol and rest in the hospital."

Cardiovascular disturbances akin to those described in beriberi have been described in the alcoholic[43] and practically all nutritional deficiencies known to occur in man have been observed in alcoholics at one time or another. It is of interest that Joffe and Jolliffe[44] have even advanced evidence strongly suggesting that the gastric achlorhydria frequently found in chronic alcoholics bears no relation to the degree or duration of alcohol addiction, and is probably due to a vitamin deficiency. Similarly, Bianco and Jolliffe[45] found the anemias of the alcoholic to be manifestations of nutritional deficiencies.

It is not to be inferred from all of this that ethyl alcohol is nontoxic. The immediate effects from the over consumption of alcohol are too well known to permit any such thesis. Incidentally, the results of acute alcoholism may differ, in some respects, in the chronic alcoholic from those observed in the normal drinker. Carroll and Goodhart[46] have described a form of total but temporary blindness associated with acute poisoning due to ethyl alcohol which occurs occasionally in chronic alcoholics, but has never been described in the normal, social drinker.

What I do wish to emphasize is that it has never been proved that any one of the so-called stigmata of chronic alcoholism is actually caused by alcoholism, *per se*. In fact, quite the contrary is true. All of those associated conditions that have been adequately investigated have been shown to be the direct result of malnutrition, with alcoholism as the conditioning or remote cause. Alcohol increases the requirements for some nutrients, and spares others. Alcohol causes gastrointestinal upsets and diminishes appetite. Also, alcoholism may induce malnutrition through the fact that money spent on alcohol is not available for the purchase of food. However, given a diet adequate to meet metabolic requirements, in a form that he can assimilate and utilize, the physical and mental health of the alcoholic can be protected.

SUMMARY

Rats, when maintained on diets deficient in certain of the B vitamins, develop a markedly increased voluntary consumption of ethyl alcohol, apparently because of the body's need for utilizable calories. When normal metabolic pathways are restored to the rat by supplying it with sufficient amounts of the missing vitamins, the animal tends to quickly lose its excessive appetite for alcohol. There is no evidence that a similar mechanism operates as a major, primary cause of alcohol addiction in man. Here, however, it must be emphasized that this possibility never has been satisfactorily investigated.

Malnutrition does play an important role in the perpetuation of excessive drinking in many alcoholics who develop deficiency states as a result of their alcoholism. As with the rat, such persons may acquire metabolic blocks and develop a reliance upon alcohol as a utilizable source of essential energy. This probability requires investigation.

More obvious is the causal relation of the painful, disabling, and embarrassing nutritional diseases in the alcoholic to the perpetuation of excessive drinking. The correction of such physical and mental ills is a prerequisite to the successful management of the alcoholism itself, and sometimes brings about a complete cure.

While alcohol is toxic to man, its known effects are acute in nature. The major, chronic, organic disorders associated with alcoholism, and often considered stigmata of alcoholism, are manifestations of nutritional disturbances. They are not peculiar to alcoholism, but occur in total abstainers who for one reason or another develop the necessary nutrient deficiencies. They can be prevented by proper nutritional management.

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The Low-Sodium Diet

SOME METHODS OF MAKING IT MORE ACCEPTABLE WITH SPECIAL REFERENCE TO THE USE OF BITTERS

By MILTON PLOTZ, M.D., F.A.C.P.*

THE LOW-SODIUM diet, often referred to as the low-salt diet, has attained a very wide sphere of popularity and usefulness. In many milder cases of cardiac decompensation, sodium restriction alone, without the use of digitalis or other medication, often suffices to prevent symptoms, enabling the patient to carry on even in the presence of severe cardiac damage. Resumption of the use of table salt in these instances, even if digitalis is given, will often result in overt heart failure. Generally speaking, it is wiser and safer to depend on dietary measures rather than to rely on diuretics to rid the body of sodium once invested. There is little probability of reaching dangerously low blood sodium levels or otherwise producing undesirable electrolyte disturbances unless there is renal disease, excessive sweating, or injudicious use of diuretic agents.

Nevertheless, this particular diet, especially among a people like ourselves, accustomed as we are to large amounts of dietary sodium chloride, is a real hardship for many patients, and often results in a feeling of deprivation and frustration. Some will resist the physician's admonitions, orders, or cajoling and return to more tempting and enjoyable foods. Our objective, recently achieved in large measure, is to make the foods offered in the typical low-sodium diet more acceptable. We have learned a great deal about how to do this since the publication of a previous paper on the subject.[1]

A common complaint is that food prepared without salt is flat, uninteresting, and lacks character. This defect can be largely corrected by the use of spices frequently avoided by patients and others concerned with preparing diets on the mistaken assumption that they are harmful. The following may all be used safely to add variety and zest to the menu.

Allspice	Marjoram
Almond extract	Mushrooms
Basil	Mustard seed
Bay leaves	Nutmeg
Cardamom	Onion
Carroway	Paprika
Chili powder	Parsley
Cinnamon	Pepper, freshly ground
Clove oil	Peppermint
Cocoanut	Pimiento
Curry	Rosemary
Dill	Saffron
Garlic	Savory
Ginger	Sesame
Honey	Sour salt (U.S.P. citric acid)
Horseradish (home prepared)	Sugar
Jams	Tarragon
Lemon juice	Thyme
Lime juice	Vanilla
Mace	Vinegar

Several herb dealers are marketing combinations of these as highly satisfactory seasonings for foods. Yeast has been toasted over hickory smoke to produce a powder greatly resembling bacon in flavor.

We have found that a significant advance in giving salt-free foods the tang or "bite" that

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they usually lack is the use of Angostura Aromatic Bitters hitherto employed almost entirely in the preparation of alcoholic drinks. The bitters pick up at once the flat taste of salt-free soups. They may be used too in salads, pies, fruit salads or mixed with low-salt cottage cheese, gravies, and puddings.

The sodium content of Angostura Aromatic Bitters is unexpectedly low. The sodium content in 100 ml is 3.88 mg; in one "dash" (1.3 ml) is 0.05 mg and in one teaspoonful 0.16 mg. The bitters can therefore be used freely, and this innovation has been accepted with relief and eagerness by nearly all patients. So far, 100 patients have been instructed to use this spice, and only seven report that they have discontinued its use after three months' trial. Of these seven, three report that they still use the bitters occasionally to improve the flavor of special foods. Despite its name, the manufacturers report that the bitters do not contain Angostura bark. The product, although produced by secret formula, is a mixture of aromatic spices such as cloves, cinnamon, mace, sweet orange peel, cardamom, with gentian in an alcoholic menstrum. The amount used will vary with taste but is usually about 1 ml to the average portion.

Some of the ways in which taste may be added to vegetables and meats are listed below:

Vegetables

Asparagus: Sprinkle with freshly grated nutmeg.

Broccoli: Add butter and lemon juice.

Corn: Add sugar and freshly ground pepper.

Carrots: These should be boiled, the water discarded, and boiled again. Mint, tarragon, or butter and chives can be used to add flavor. Carrots should not be used at all in very restricted diets.

Cauliflower: Add butter or cream sauce seasoned with nutmeg or Angostura Bitters.

Cucumbers: May be diced and boiled in cream sauce with nutmeg, sliced raw very thin and then marinated in any vinegar.

Eggplant: Peeled, diced, boiled, and drained. Add tomatoes, bay leaf, and oregano.

Green beans or lima beans: Add nutmeg or savory and butter.

Sweet potatoes or yams: Boil and peel, then bake sliced and covered with a mixture of brown sugar and rum.

Leeks: Sprinkle with freshly grated nutmeg.

Mashed potatoes: Add freshly grated onion and nutmeg.

Mushrooms: Saute in butter with chopped onion.

Onion: Boil with clove and thyme.

Peas: Boil in sweetened water, drain, and add butter and chopped or powdered mint.

String beans: Marjoram improves the taste greatly.

Tomatoes: May be broiled, halved, with butter and a pinch of oregano or basil. May be stewed with bay leaf, onion, and oregano. Angostura Bitters add flavor to tomatoes, raw or cooked.

Meats

Goulash: Onion, bay leaf, tomato, sweet paprika, pepper, rosemary leaves or oregano, and Angostura Bitters are suggested for flavoring.

Lamb chops: Rub chops with pepper and ginger before broiling.

Roast beef: Rub meat with pepper and ground ginger. Put 1 large bay leaf in roasting pan and baste every 15 minutes.

Veal chops: Rub chops with pepper and saffron. Brown a little margarine, then add a little water and simmer until done.

Veal stew: Onion, bay leaf, powdered mace, celery leaves, and bitters to flavor.

Breads

"Salt-free breads" which are generally satisfactory are available in almost all large cities or may be ordered by mail. Toasting the bread makes it very palatable. The toasting process will improve other bread products. In addition unsalted Italian breadsticks and even pretzels can now be bought.

SOME WARNINGS

Both butter and oleomargarine are usually sold salted. The patient should insist on unsalted varieties. Nearly all canned foods and soups contain salt as do some frozen foods. Here, too, the purchaser should learn to read labels warily. Celery, garlic, and onion salts, it should be remembered, contain huge amounts of sodium. In addition, many "flavor improvers" contain sodium. Special foods offered as "salt-poor" should contain statements as to their actual salt content. Edam and Port Salut cheeses bought as low-sodium cheeses in a large department store were found to have 0.39 and 0.44 meq of sodium per gram. Such foods could not of course be eaten freely in a salt-restricted diet.

Some of the artificial sweeteners now on the market contain sodium; sodium-free substitutes are available and should be used. Many candies contain salt and the admonition to read the label applies here as well. This is particularly true of candies containing chocolate, especially the Dutch process chocolate.

COMMENT

A cook who reads one of the several very satisfactory cook books now on the market and uses some ingenuity of her own can easily make life more agreeable for the patient. The

author and his staff would be glad to receive further suggestions from the readers of this paper.

There is little likelihood that the low-sodium syndrome will develop in patients who follow a diet such as this unless they are getting diuretics in addition or are losing sodium in other ways. The physician of course, must be on the alert for this condition in patients to whom he is giving mercurials or other diuretics.

Angostura Bitters were found to be an exceptionally acceptable flavoring agent for daily use over a three-month trial period for 93 out of 100 patients; three patients had occasional use for it, and only four discontinued its use.

The low-sodium diet is a useful one and is now deservedly popular. With the exercise of some ingenuity, the diet may be made quite palatable. Specific suggestions are given in the article.

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Effects of Iron Treatment of Anemia in a Tropical Area

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THE IMPORTANT role that malnutrition plays in hookworm disease has long been recognized although the part that specific nutrients may play has not been seriously studied. It does seem generally accepted that the anemia is primarily an iron-deficiency anemia produced by chronic blood loss, and iron therapy has long been used in its treatment.[1] Rhoads and his associates[2] and Cruz[3] demonstrated that the removal of the parasites brought about only slight improvement whereas iron therapy, without removal of the parasites, was effective. Large amounts of iron were used. Rhoads *et al.* gave 4 to 6 g of ferric ammonium citrate per day. Cruz[4] reported that the minimum effective daily doses of various iron preparations varied from 0.6 g of ferrous ammonium citrate to 0.2 g of ferrous phosphate.

Since that time there have been numerous reports of the effectiveness of iron treatment. Payne and Payne,[5] for example, showed that in children with 4,500 or more hookworm eggs per cc of feces, the largest gains in hemoglobin upon administration of 2 g of ferrous carbonate daily were in those children who were originally the most anemic. Five months after the therapy was stopped, the hemoglobin concentrations had essentially returned to pretherapy levels. Hynes *et al.*[6] working with Indian army recruits, reported that 0.2 g of ferrous sulfate per day cured all of the anemias in four months and that the hookworm infections did not interfere with hemoglobin regeneration. A correlation was found between the degree of infection and low hemoglobin only in the more undernourished. Cruz and Pimento[7] concluded that the symptoms remaining after treatment of the anemia are so minor that the anemia might be considered as the disease itself. Doses of 0.21 to 0.37 g equivalent of iron maintained the response over long periods of time, but the hemoglobin seldom rose over 11 g/100 ml. Gerritsen and Walker[8] concluded from their study of the treatment by iron of the hypochromic anemia of pregnant Bantu women infected with hookworms that the hemoglobin levels could be largely restored to normal by such therapy alone without either improvement in the diet or removal of the parasites.

Evidence has also accumulated to support the view that until the hookworms are eliminated, the associated anemia cannot be completely cured. Day and Ferguson[9] reported that in cases of decided anemias, iron treatment was unsatisfactory in adult Egyptians unless they were first dewormed. Otto and Landsberg[10] studied the relation of diet to resistance to infection with hookworm in dogs and found that the only safe course of treatment was to remove the worms. When the diet was poor with respect to vitamins and protein, iron therapy could not bring about recovery, but when the diet was adequate, iron was effective in preventing severe hookworm

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infections. Trowell[11] found that iron was ineffective in improving the deficiency associated with hookworm infections after a "stationary stage" in hemoglobin was reached. Lehmann[12] gave 2.6 g of ferrous sulfate per day and although hemoglobin values increased during six weeks, they did not return to normal limits without treatment with anthelmintics. He concluded that, although iron may produce a normochromic blood picture, it will not fully cure an iron deficiency of that nature and that the limit of the recovery with iron without prior removal of the parasites was reached when the hemoglobin attained a level of 9 to 12 g/100 ml. He also reported that the iron-deficiency anemia may respond favorably to the removal of the hookworms without special therapy. Smillie and Augustine[13] pointed out in 1925 that it is not the incidence, but the intensity, of the infestation that determines the seriousness of the hookworm problem. If the nutritional state of the individual also determines the degree of anemia developed, then this parameter of the problem must also be considered relative to the severity of the infestation. When the parasites cannot be controlled, it is important to treat the severe cases of anemias and to employ any possible means of preventing the development of debilitating anemia. We may conclude that published information about hookworm anemia warrants the belief that, as a rule, administration of adequate amounts of iron will greatly ameliorate the severe anemias associated with ancylostomiasis. The response to iron may be in part determined by the nutritional state of the individual and by the diet taken at that time.

In order to evaluate the problem in any locality, it is necessary to know the amounts of iron which have to be supplied. If the amounts prescribed by Cruz[4] or the amounts used in current practice represent the minimum necessary, the responsibility for the anemia would not appear to rest upon the public health nutritionist. These amounts are far above those that could usually be supplied by foods. On the other hand, if small doses of iron are sufficient or useful, the fortification of foods with iron and/or nutrition education programs might be useful.

The studies reported in this paper were undertaken to determine the minimum amounts of iron which are effective in controlling the anemia of school children in Iquitos, a town on the banks of the Amazon in the Peruvian rain forest. Cornejo *et al.*[14] have previously reported that 93 per cent of the people examined in Iquitos had intestinal parasites and that 64 per cent had hookworms. Dietary surveys in this area of Peru[15,16] have shown that although many nutrients are consumed in relatively small amounts, the iron intakes are reasonably satisfactory when compared to the current recommendations of the Food and Nutrition Board of the National Research Council.[17] They estimated the mean intake to be 12 mg per day; the amount recommended for the average adult. Nevertheless, anemia is widespread and, undoubtedly, it is related in large part to hookworm disease.

METHODS

Two similar groups of approximately 50 girls each took part in the first study. They constituted the entire enrollment of one of the schools of Iquitos. The ages ranged from six to fourteen, averaging nine years. Prior to the beginning of the study the girls were given physical examinations, qualitative and quantitative parasite examinations, and the families of some of the children were asked to cooperate in a dietary survey. Blood samples were obtained for hemoglobin determinations at the beginning of the study and again after 6 and 14 weeks of therapy as well as three and eight months after the iron administration was discontinued. For the 14 weeks of the test, a nurse visited the school six days each week to administer pills containing 50 mg of iron as ferrous sulfate or a placebo. Records were kept of attendance, and care was exercised to assure that the pills were swallowed. The iron was administered at the same time each day, during recess at 9:30 a.m. The usual dietary practices of the subjects were not altered.

The second study carried out one year later with a similar group of children was conducted in a like manner. Two groups of children received 15 or 30 mg of iron each day for 12 weeks.

The zinc sulfate method of Faust *et al.*[18] was employed for the qualitative recovery of parasite eggs, larva, cysts, or trophozoites. The method of preparing a standard fecal smear developed by Beaver[19] was used in the quantitative estimation of the hookworm load. The species of hookworm, i.e., *Ancylostoma duodenale* or *Necator americanus* was not determined.

RESULTS

The results of the qualitative parasite examinations which were made on 91 of the girls are given in Table I. Multiple parasitic infections were the rule; 93.5 per cent of the girls were found to be harboring two or more different helminths, while only one girl was found to be free of both worms and protozoa. Twenty-one girls had as many as four different types of parasitic worms and 26 had one or more protozoan types. The most common protozoan infection was from *E. coli*; 12 of the 13 cases with *E. coli* had hookworm infections as well. In all, 83 cases or 91.2 per cent of the total examined were found to have hookworm infections. As Gonzales-Mugaburu[20] has pointed out, a re-examination of 75 per cent of the same group three months later indicated that the rate of hookworm infection is probably as high as 98 to 99 per cent. The infection rate of *Ascaris* and *Trichuris* was also high, being 75 per cent and 81 per cent, respectively. Seventy-three examinations were made for *Enterobius vermicularis* (pin worm) by the "scotch tape" technic; all were negative.

TABLE I

Qualitative Parasite Spectrum of Iquitos School Children

	Number infected	Per cent infected
Helminths		
Ascaris lumbricoides	68	74.7
Trichocephalus trichiurus	74	81.3
Hookworm	83	91.2
Stronglyoides stercoralis	28	30.7
Protozoa		
Entamoeba coli	13	14.3
Entamoeba histolytica	4	4.4
Chilomastix mesnili	7	7.7
Giardia lamblia	2	2.2
Balantidium coli	1	1.1
Iodamoeba buetschlii	1	1.1

Multiple Parasite Infections

Number of multiple infections	0	1	2	3	4
		Number of children			
Helminths	1	5	26	38	21
Protozoa	65	22	4	0	0

At the beginning of the first study the mean hemoglobin concentrations of the two groups were 10.32 ± 1.862 standard deviation and 9.39 ± 1.751 g/100 ml for the control and experiment group respectively. Included in these means are values from 4.02 to 13.75 g/100 ml. With therapy of 50 mg of iron per day, the mean hemoglobin of the experimental group increased to 10.21 ± 1.66 g during the first six weeks and was not greatly different from this value after 14 weeks of treatment with iron.

When the response to therapy is related to the initial hemoglobin levels, the effect of iron therapy on the anemia is clear. In Table II is given a distribution of the mean hemoglobin responses, with initial hemoglobin levels of the subjects. The children who were the most anemic demonstrated the greatest hemoglobin response and this response was maximal during the first six weeks. The children with an initial hemoglobin over 10 g showed a slight decrease as a group whereas the girls with the low hemoglobin concentration of less than 8 g, initially averaging 6.88, showed a regeneration of 2.17 g to attain a new mean of 9.05 g in 14 weeks. In the same time the group of girls with initial hemoglobin concentrations between 8 and 9 g achieved an average hemoglobin response of 2.00 g. This graded change in hemoglobin with therapy is shown graphically in Figure 1 in which hemoglobin change is plotted for each hemoglobin subgroup after 6 and 14 weeks of iron therapy as well as three and eight months after treatment.

The control group showed, on the average, no significant change in hemoglobin values. It is of interest, however, that the most anemic children in the control group showed a tendency to improve during the study. The average hemoglobin of the iron-treated children

TABLE II.
Hemoglobin Levels with Time During and After Iron Therapy with 50 mg Iron per Day

	Control group			Experimental group		
	No.	Mean hemoglobin *g/100 ml*	Standard deviation	No.	Mean hemoglobin *g/100 ml*	Standard deviation
I. Initial values						
(a) Total group	50	10.32	±1.862	54	9.39	±1.751
(b) Subgroup less than 8 g	7	6.87	±2.852	11	6.88	±1.093
(c) Subgroup 8–9 g	4	8.89	—	10	8.50	±0.247
(d) Subgroup 9–10 g	7	9.47	±0.336	13	9.51	±0.085
(e) Subgroup over 10 g	32	11.39	±1.036	21	11.15	±0.623
II. At 6 weeks						
(a) Total group	50	10.29	±2.303	54	10.21	±1.166
(b) Less than 8 g initial	7	7.14	±3.243	11	8.83	±1.150
(c) 8–9 g initial	4	9.21	—	10	10.55	±1.009
(d) 9–10 g initial	7	9.78	±3.91	13	10.30	±0.730
(e) Over 10 g	32	11.22	±1.127	20	10.89	±0.610
III. At end of 14 weeks						
(a) Total group	50	9.95	±1.709	54	10.36	±1.096
(b) Less than 8 g initial	7	7.63	±3.393	11	9.05	±0.944
(c) 8–9 g initial	4	9.16	—	10	10.30	±0.887
(d) 9–10 g initial	7	8.91	±1.160	20	10.97	±0.610
IV. 14 weeks after therapy						
(a) Total group	31	10.00	±1.617	32	10.30	±1.602
(b) Subgroup less than 8 g	6	8.40	±4.207	6	8.70	±4.525
(c) Subgroup 8–9 g	3	8.78	—	6	9.96	±1.168
(d) Subgroup 9–10 g	3	10.05	—	8	10.69	±4.161
(e) Subgroup over 10 g	19	10.64	±1.329	12	11.03	±0.477
V. 8 Months after therapy						
(a) Total group	16	10.38	±0.931	25	9.06	±1.844
(b) Subgroup less than 8 g	2	8.67	—	4	6.60	—
(c) Subgroup 8–9 g	—	—	—	7	8.48	±1.874
(d) Subgroup 9–10 g	3	9.64	—	6	9.73	±0.857
(e) Subgroup over 10 g	11	10.89	±0.579	8	10.28	±0.670

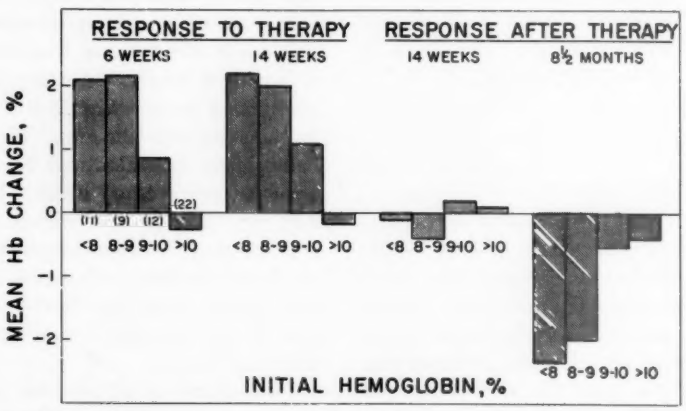

Fig. 1. Hemoglobin response at various times related to the original hemoglobin level.

was maintained at the higher levels for at least 14 weeks after treatment was stopped, but after eight months without iron supplements the hemoglobin levels were back to about the initial values. The most anemic, who had shown the greatest response, fell the most dur-

ing this period so that the general situation became about the same as at the initiation of the study.

This return to the pretherapy levels might be expected if the degree of anemia were related to the hookworm load and the need for extra iron would be felt as soon as the newly acquired stores were depleted. No measures were taken to control infestation during the study. The correlation in Figure 2 shows that as the number of eggs or severity of infection increased, the hemoglobin values were lower, and the degree of anemia correlates reasonably well with the degree of hookworm infestation. As expected, the children with heaviest loads also showed the greatest decline in hemoglobin after therapy was stopped. Nevertheless, 50 mg of iron per day permitted a considerable hemoglobin response in the frankly anemic children.

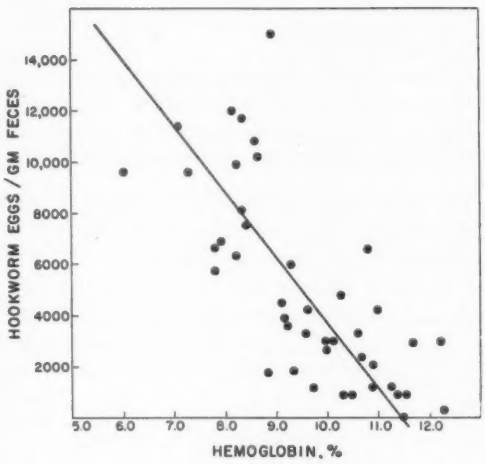

Fig. 2. The relationship between the severity of the parasitosis and the degree of anemia.

The second study was designed to define further the minimal requirement for iron under existing dietary and environmental conditions. One group of 58 girls was given 15 mg of iron as $FeSO_4$ per day while the second group of 56 girls was given 30 mg. The hemoglobin values initially, after six weeks and after 12 weeks of treatment are shown in Table III both for the average of the groups and the subgroups divided according to the initial hemoglobin values. The results are essentially the same as in the previous study. The more anemic children showed the greatest response. This was similar in the two groups although actually the hemoglobin level of the 15 mg group increased somewhat more than the 30 mg group. The magnitude of the response is similar to that obtained with 50 mg of iron in the previous study. The group of children with hemoglobin levels above 10 g/100 ml did not respond to iron

TABLE III

Hemoglobin Levels with Time; 15 and 30 mg of Iron per Day

	15 mg Fe			30 mg Fe		
	No.	Mean hemoglobin *g/100 ml*	Standard deviation	No.	Mean hemoglobin *g/100 ml*	Standard deviation
I. Initial values						
(a) Total group	58	10.15	±1.589	56	9.72	±1.649
(b) Group less than 9 g	11	7.82	±0.849	17	7.66	±0.951
(c) Group between 9–10 g	15	9.51	±1.000	10	9.66	±0.290
(d) Group over 10 g	32	11.26	±0.900	29	10.96	±0.651
II. 6 weeks						
(a) Total group	56	11.09	±1.048	56	10.91	±1.285
(b) Less than 9 g/100 ml	9	10.76	±1.000	17	9.95	±0.938
(c) 9–10 g/100 ml	15	10.96	±0.907	10	10.88	±1.037
(d) Over 10 g/100 ml	32	11.24	±1.080	29	11.48	±1.105
III. 12 weeks						
(a) Total group	49	10.63	±0.966	41	10.86	±1.185
(b) Less than 9 g/100 ml	9	10.95	±0.913	9	9.69	±1.255
(c) 9–10 g/100 ml	12	10.41	±0.832	7	10.66	±0.538
(d) Over 10 g/100 ml	28	10.62	±1.004	25	11.34	±0.762

therapy although practically the whole population could possibly be classified as anemic.

DISCUSSION

The primary public school children used in these studies may be considered typical of the juvenile population of Iquitos. The sanitary conditions under which the people of Iquitos live would certainly be no worse and may be better than those of smaller towns or of the rural areas of the jungle. Thus, the parasitic and nutrition situation of Iquitos may be typical of much of the jungle area of the Amazon Basin and perhaps of many other tropical areas. Sixty-three per cent of the subjects of the first experimental group had hemoglobin concentrations less than 10 g/100 ml and 20 per cent had less than 8 g/100 ml. Of the entire 218 girls who took part in these studies, 48 per cent had hemoglobin concentrations less than 10 g/100 ml.

The studies have demonstrated that extradietary iron of a magnitude not far above that attainable by food enrichment and diet guidance is effective to a large measure in overcoming the frank anemia. There was little difference found in the response to the three different levels of intake of iron tested although it is not known whether protection for three months without iron supplementation, as was given by 50 mg of iron daily, would also be provided by the smaller supplements. All of the severely anemic children showed a hemoglobin response that was generally maximal within six weeks of treatment. Since equivalent responses were obtained with either 15, 30, or 50 mg of iron, the supplement required in addition to the amount supplied in the diet appears to be somewhat less than 15 mg of iron per day.

A typical scatter diagram relating the individual initial hemoglobin values with the response obtained is shown in Figure 3. It is clear that when the hemoglobin levels were below approximately 10 g/100 ml, iron was limiting hematopoiesis. Above this level no response was obtained. This is the range that Trowell[11] and Lehmann[12] have indicated as the stationary stage of hemoglobin regeneration without primary deworming. Whether nutritional, parasitic, or other environmental factors

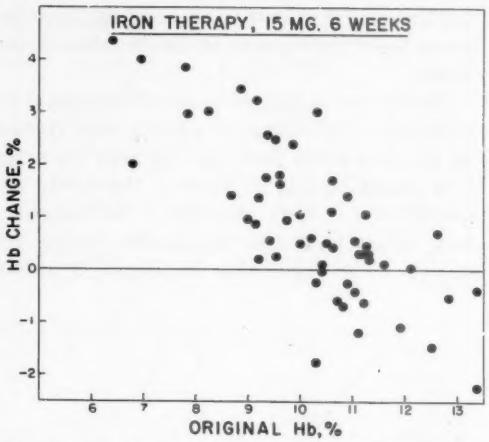

Fig. 3. The hemoglobin response of the individual children compared to their original hemoglobin level.

are involved in the failure to achieve normal hemoglobin levels remains to be determined. Further studies are now under way.

It is of interest that the control group of children without iron supplements also showed a hemoglobin response related to the original level of hemoglobin (Fig. 4). This would suggest that the amount of iron in the diet is just marginal. Adaptive mechanisms which allow more efficient utilization of dietary iron may become increasingly effective and thus prevent partially the development of severe anemias in many of the children. The differences in the height and slope of the regression in Figures 3 and 4 are evident.

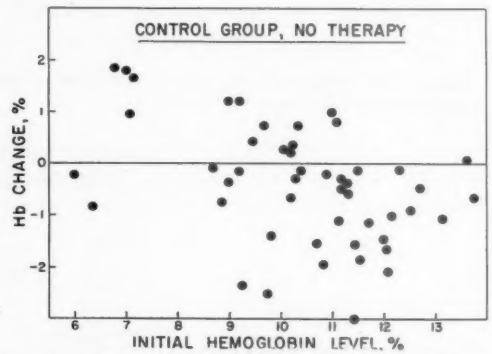

Fig. 4. The change in hemoglobin level of the children who received no therapy related to their original hemoglobin level.

Although iron therapy cannot be considered

as a cure of ancylostomiasis, the prevention of severe anemias would appear to be extremely useful until more effective methods of preventing the infestations are available. The amount of iron required under the conditions of this study are somewhat above the average intake of 12 mg and probably less than this amount plus 15 mg which was the lowest supplemental level used. Whether food iron is equally or less effective than the ferrous sulfate used as a supplement remains to be seen. In any event the results are encouraging and relatively small increases in dietary iron appear to be of considerable benefit. It seems likely that a means must be found for the fortification of foods with iron but that the present methods of enriching flour and rice may not be effective. The intake of bread is relatively small in Iquitos and probably much less away from the centers of population. Rice is more of a staple food. However, the enrichment of both bread and rice with standard enrichment formulae would be expected to supply only about 3 mg of iron daily. It is rather doubtful that this would be an effective supplement and either changes in the formula or more effective carriers may be required.

SUMMARY

Girls in primary public schools served as subjects in a study to determine the iron requirements in the Peruvian jungle area. The girls were heavily infested with a variety of intestinal parasites. Seventy-five per cent of the subjects showed Ascaris, 91 per cent hookworm, and 81 per cent Trichuris. Protozoan cysts were found in 31 per cent. The hemoglobin levels ranged from 4.0 to 13.8 g/100 ml with an average value of 9.8. Approximately half of the girls had hemoglobin levels less than 10 g/100 ml. Quantitative studies showed that the degree of anemia below 10 g/100 ml was related to the hookworm load.

Four groups of approximately 50 girls received respectively 0 (placebos), 15, 30, or 50 mg of iron as ferrous sulfate daily for periods up to 14 weeks. The hemoglobin response was essentially maximal within six weeks. The most anemic children showed the greatest response with average increases of 3 to 4 g of hemoglobin per 100 ml. Hemoglobin levels above 10 g/100 ml were not increased by iron treatment. All levels of iron used appeared to be equally effective.

When iron treatment was stopped, the group of children which had received 50 mg of iron daily maintained their hemoglobin levels for three months, but had returned to pretreatment levels within eight months. The other groups were not studied after therapy.

The average dietary intake of iron for the subjects was estimated to be approximately 12 mg per day and the total iron requirement to maintain the hemoglobin levels at approximately 10 g/100 ml would appear to be somewhat less than 25 mg per day. Thus, relatively small increases in the iron intake proved to be beneficial. It is concluded that means should be sought, by fortification and/or dietary instruction, to increase the iron intake.

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Serum Cholesterol Levels in School Children from Three Socio-Economic Groups

By NEVIN S. SCRIMSHAW, PH.D., M.D.,* ALAN BALSAM, B.A.,† AND GUILLERMO ARROYAVE, PH.D.‡

THE SERUM cholesterol levels of rural low-income adults in both Guatemala[1] and Costa Rica[2] have been shown to be significantly lower than middle and upper income persons in urban areas of the United States and Guatemala matched for age and sex. Reports of a comparable nature based on work in Italy,[3] Spain,[4] South Africa,[5–8] and Japan[9] as well as studies with experimental human diets[3,10–16] have given similar evidence of the role of environmental factors in determining the mean cholesterol levels of population groups. In these studies the factor receiving greatest attention has been the difference in habitual diets,[9,13] particularly the relative amounts of protein of animal origin, and fat.[7,8,17]

Serum cholesterol levels appeared to be low in children at birth[7,18,19] and at this time, to be independent of the diet, race, and cholesterol level of the mother.[5] They have been reported to rise during the first two years of life to levels within the adult range.[18–20] During childhood and adolescence, most observers have found no consistent variations with either age or sex.[16,21–25] In view of the marked differences in serum cholesterol levels among adults in different socio-economic groups in Guatemala, it was of great interest to determine whether school children show the differences in serum cholesterol levels which characterize their parents.

This report presents the total serum cholesterol levels of 288 Guatemalan school children selected from three distinct economic and occupational groups of differing dietary habits.

MATERIAL

Economic and Social Status

Boys and girls 7 to 12 years of age were selected at random from the following three types of Guatemalan primary schools:

Group I: Urban Private School—the fathers of these children were mainly business and professional men in Guatemala City. Only children having at least one Guatemalan parent were included. Many of the parents in this group had been examined previously.[1]

Group II: Urban Public School—the fathers of the children in this group worked as mailmen, policemen, truck and bus drivers, and at other unskilled and semiskilled labor. They lived in a relatively poor district of Guatemala City.

Group III: Rural Public School—the fathers of most of these children worked as agricultural laborers on nearby farms and coffee plantations or on their own small plots of land. They lived in and around the rural village of San Miguel Dueñas, Department of Guatemala, and their parents were representative of the other rural Guatemala adults studied previously.[1]

Dietary Habits

No precise dietary information was available for most of the school children studied, but the diets of the parents of these children, or of adults of comparable socio-economic groups were analyzed in detail and have been summarized in Table I. The total calories,

From the Institute of Nutrition of Central America and Panama (INCAP), Guatemala City, Guatemala, C. A. INCAP Scientific Publication I-70.

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TABLE I

Dietary Estimates for the Study Groups

Group No.		Calories	Protein, g/day			Fat, g/day			% Calories from fat
			Animal	Vegetable	Total	Animal	Vegetable	Total	
I	Urban upper-income	2,462	39	30	69	46	56	102	37
II	Urban lower-income	1,585	10	37	47	13	14	27	15
III	Rural lower-income	2,283	6	61	67	9	14	23	8

percentage of calories from fat, and the proportions of animal and vegetable protein are indicated for each of the three groups. The technics employed by INCAP for collecting and calculating the dietary data have been previously cited.[1]

The dietary pattern of Group I was based on seven-day diet histories obtained in November 1954, from 15 mothers of children[26] in the private school included in the present study.

Similar dietary information for Group II has been calculated from the diet histories of 15 families in the nearby town of Amatitlán.[27] Their diets correspond closely to those of the four- and five-year-old pre-school children recently studied in a poor district of Guatemala City.[28]

Dietary information for Group III has been published previously.[1] The figures in Table I are averages for four villages in the immediate vicinity of San Miguel Dueñas.[29–32]

METHODS

Eight boys and eight girls were selected at random from each age group from seven through twelve, in three different schools. Children obviously ill with an acute or chronic disease were excluded. At least 0.5 ml of blood was extracted from the fingertip. The serum was separated and frozen within eight hours of collection of the blood and analyzed within ten days.

Total serum cholesterol was determined by the method of Abell *et al.*,[33] with the modification that all quantities of samples and reagents were reduced by one-half so that sufficient serum (0.26 ml) could be obtained from fingertip-blood samples. The significance of the

TABLE II

Height and Weight and Skin-Fold Thickness of Guatemalan School Children*
(8 Children per Group)

Age (years)	Urban upper-income						Urban lower-income						Rural lower-income					
	Height		Weight		Skin-fold		Height		Weight		Skin-fold		Height		Weight		Skin-fold	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Boys																		
7	126.0	4.1	26.8	5.3	7.0	3.2	113.4	3.5	20.2	2.5	6.7	2.0	112.2	6.5	20.4	2.5	5.5	1.1
8	127.1	4.2	26.6	4.2	6.8	1.1	116.5	6.0	21.4	2.4	6.4	1.2	113.8	3.8	21.1	1.7	6.8	1.7
9	133.7	3.8	32.3	7.7	8.5	1.8	123.3	4.7	23.4	2.9	6.3	1.7	118.5	8.8	22.2	2.8	4.4	1.3
10	135.9	3.7	31.7	4.6	10.2	3.6	124.6	7.6	25.6	3.8	5.8	1.2	124.6	5.9	24.5	3.2	6.0	2.4
11	139.4	4.0	33.5	3.3	7.9	2.9	129.0	7.4	26.8	4.5	5.4	1.1	127.8	6.5	26.4	2.9	6.5	2.9
12	148.8	3.5	43.0	4.5	10.9	3.9	135.6	4.6	31.4	3.4	6.8	0.7	132.6	6.2	28.1	4.0	4.9	0.9
Girls																		
7	120.4	5.9	23.7	3.6	8.1	2.6	113.0	5.5	19.3	2.2	6.7	1.4	111.1	5.3	20.6	2.8	6.5	2.0
8	126.2	6.9	26.8	4.1	8.8	1.3	117.1	6.2	21.3	3.4	7.4	1.7	113.8	4.5	19.8	2.0	6.4	1.7
9	130.4	4.0	32.0	3.8	10.1	2.2	122.0	5.5	22.4	3.2	5.8	0.9	120.8	4.9	21.7	1.8	5.8	0.9
10	135.8	5.3	36.0	4.3	12.2	1.9	127.9	10.0	24.5	3.8	6.6	2.0	125.9	5.3	25.8	5.0	6.6	3.2
11	142.3	5.0	38.0	6.2	11.0	3.9	131.2	3.2	28.4	3.3	6.7	3.4	134.1	8.5	30.8	5.6	8.0	3.3
12	155.8	7.1	46.0	9.0	9.3	3.7	137.3	3.2	30.8	2.5	7.5	2.0	131.6	6.7	29.7	3.2	6.9	2.1

* Height in cm, weight in kg, and skin-fold thickness in mm.

S. D. = standard deviation.

differences among the cholesterol values obtained was determined by the *t*-test.

Height, weight, and general nutritional status were determined at the time the blood samples were taken.* Measurements of the thickness of the skin-fold of the posterior surface of the upper arm were made according to the recommendations of Brožek *et al.*[34]

RESULTS

The values obtained for height, weight, and skin-fold thickness are shown in Table II. These values indicate that the upper-income urban children were taller, heavier, and had more subcutaneous fat than either the urban or rural lower-income groups. The differences between the latter two groups were not statistically significant although the urban children showed slightly higher values for all three measurements.

The lower-income children, both urban and rural, had frequent follicular hyperkeratosis and mild tongue changes suggestive of nutritional deficiency. The serum cholesterol results obtained are summarized in Table III. The average cholesterol values were significantly different ($P < 0.01$) among each of the three school groups for both boys and girls. There was no consistent tendency for the values to increase with age during the period studied. Moreover, the cholesterol differences between boys and girls were not significant for either the upper-income urban or the lower-income rural groups. However, in the urban public school group the average sex difference in cholesterol was significant at the 5 per cent level.

DISCUSSION

The data clearly demonstrate that the environmental factor or factors responsible for the differences in serum cholesterol between upper-income and lower-income adults in Guatemala also affect the serum cholesterol levels of children of school age. In view of these results, and the finding that regardless of the status of the mother serum cholesterol levels are low at birth and rise rapidly during the first few days,[18–20] it is possible that still younger children would show this difference.

It is of special interest that the relatively small dietary and other differences between the lower-income urban and rural groups should be reflected in significant differences in serum total cholesterol. Apparently, the mechanism responsible for maintaining serum cholesterol levels is sensitive to relatively small changes in the environment; whether or not these are dietary cannot be concluded from the present

* These samples were collected jointly with Mr. Roger A. Feldman for a parallel study of serum pseudocholinesterase levels. The collection of blood samples in Group I was made possible through the kind cooperation of Mr. Robert B. McVean, Director of the *Colegio Americano de Guatemala*.

TABLE III

Serum Cholesterol Levels of Guatemalan School Children*

(8 Children per Group)

Age (years)	Boys						Girls					
	Urban upper-income		Urban lower-income		Rural lower-income		Urban upper-income		Urban lower-income		Rural lower-income	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
7	205.9	19.7	139.7	25.7	118.5	19.2	192.1	25.2	154.0	26.6	121.4	12.1
8	173.6	22.6	129.6	22.2	107.5	23.4	172.8	30.0	157.3	31.7	108.6	23.2
9	180.2	29.8	142.2	35.1	115.1	35.3	184.9	33.1	160.7	33.2	126.7	33.0
10	181.1	24.0	135.2	16.0	135.8	17.4	196.2	36.7	149.2	38.5	140.9	27.1
11	201.9	31.2	149.3	38.1	122.5	18.4	194.5	25.0	153.5	29.2	129.4	19.0
12	180.5	21.5	162.0	27.8	127.3	22.4	185.2	31.0	161.4	23.4	139.1	13.2
Total	187.2	26.8	143.0	28.9	121.1	24.0	187.6	29.9	156.0	29.5	127.7	24.0

* Expressed in mg/100 ml.

data. However, children should be suitable experimental subjects for determining the specific factors responsible for the observed differences in cholesterol among socio-economic groups.

It should be noted that the children with relatively low serum levels of cholesterol belong to the same socio-economic groups in which the severity of atherosclerosis and frequency of myocardial infarction are relatively low.[35]

Except for the work of Strong *et al.*[36] relatively little attention has hitherto been paid to atherogenesis in children, but the present findings suggest that such studies may prove useful. In view of its potential importance in relation to the development of atherosclerosis, these investigations should also include determinations of serum cholesterol.

SUMMARY

Total serum cholesterol was determined in eight boys and eight girls selected at random for each age from seven through twelve in schools with children from the following three population groups: urban upper-income business and professional families, urban lower-income families living in a poor district of Guatemala City, and lower-income families in a rural village. The former consumed about 69 g of protein per day and received 37 per cent of their calories from fat as compared with 47 g and 15 per cent for the urban lower-income and 67 g of protein and 8 per cent of fat calories for the rural group. The amount of animal protein consumed by the three groups was 39, 10, and 6 g respectively. The urban children tended to be heavier and taller; their skin-folds over the mid-triceps area were thicker. The serum cholesterol levels showed no age differences within groups. The average cholesterol values for boys were: urban upper-income, 187.2 mg/100 ml (Standard Deviation: 26.8); urban lower-income, 143.0 mg/100 ml (S.D. 28.9) and rural lower-income, 121.1 mg/100 ml (S.D. 24.0). The corresponding values for girls were: 187.6 (S.D. 29.9); 156.0 (S.D. 29.5) and 127.7 mg/100 ml (S.D. 24.0). All of the serum cholesterol differences among the groups were statistically significant.

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Dietary Survey on Rarotonga, Cook Islands*

III. FEEDING PRACTICES AND GROWTH OF RAROTONGAN CHILDREN FROM BIRTH THROUGH SIX YEARS

By PEGGY CROOKE FRY, B.S., M.P.H.

A STUDY was made of the feeding practices and growth of young children at the same time as the recently reported family dietary survey in two villages on Rarotonga.[1,1a] Although it was known that the New Zealand government had initiated a child-care program in the early 1930's, little information on existing Maori customs was available at the beginning of the nutritional survey in 1953–54. Hence, it became important to try to determine the extent of the influence of European ways and the amount of traditional customs still prevailing among Polynesian mothers. In addition, some aspects of the growth of children on Rarotonga, as compared with that of children on American Samoa (Polynesia), and of children from European stock (Iowa, U.S.A.), are presented to give a clearer picture of the adequacy of the Rarotongan diets for optimal growth and health.

The Rarotongan Official Census of 1951 (Table I[1a]), shows that 56.4 per cent of the total island population is under 20 years of age, 71.2 per cent below 30, and 90.1 per cent under 50 years of age. Young adults and children form the major components of the Rarotongan population. It was found that of the 41 households reported on previously, 54 per cent (22) had one or more children under two years of age, and 83 per cent (34) had one or more children under seven years.

The Official Report on the Cook Islands[2] stated that the infant mortality rate in 1951 was 137.61 per 1,000 live births. Tuberculosis in all forms was the leading cause of death on Rarotonga (300/1,000 population), the other major diseases resulting in fatality were pneumonia and gastroenteritis (145/1,000 and 89/1,000 population, respectively). The average mother between the age of 16 and 55 had 5.2 living children, although only 0.23 per cent of the children were born to mothers between 16 and 19 years of age. Since birth certification procedures on Rarotonga were not complete, these figures can be questioned.

METHODS

The two villages, Arorangi and Titikaveka, in which the children lived, have been described in the previous publications, as have the typical family meal patterns, the methods of gathering, and treatment of family dietary data. During daily visits to the homes for periods of seven to ten days, information was obtained concerning the mothers' attitudes in regard to child feeding, as well as qualitative daily food intakes of all children under seven years of age used in the study. The statements that are presented concerning present-day practices and children's activities on Rarotonga are based on observations and data gathered by the writer during an eight months' residence on Rarotonga.

Physical examinations and weighing of food portions for the children in each family were not feasible. Weight measurements on 100 children and stature measurements on 74

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children were secured. Seventy of the 100 subjects were from the family dietary survey, while a concurrent physical anthropological study of school children[3] added the remaining 30 children under seven years of age.

TABLE I

Present-Day Infant Feeding Practices

Age	Nutrient source
From birth until 4–5 months	Mother's milk
4 to 5 months until 9 months	Mother's milk Papaya soup Cooked and mashed *taro*, *kumara*, or banana with coconut cream Bread softened in tea
9 to 10 months until 12 months	Tea with sugar Fish, shellfish, or canned meat Cooked unmashed *taro*, *kumara*, breadfruit or cassava Ripe bananas Coconuts Bread
12 to 14 months	Usual adult diet—all the foods above plus *rukau*

Interviews with older Maoris in the villages provided basic knowledge of the practices of the previous generation. There is, of course, a tendency to question the reliability of such statements. The generalizations presented here are the points on which there was common agreement; any assertions which were at variance with the procedure as described by the majority have been omitted.

RESULTS

Traditional Infant Feeding

At the time of the beginning of administrative concern, it seems to have been the prevailing custom among Maori women on Rarotonga to breast-feed infants up to the age of nine to ten months, with no other foods being offered to the child until this age. The infants were fed whenever they cried, day or night, since they usually slept with the mother and were with her throughout the day.

At about nine months of age, the flow of breast milk was diminishing in supply, and supplementation began with the flesh of immature coconuts. At this stage, the coconut flesh is soft and moist and can be scraped and mixed with coconut water. Other foods introduced at about the same time included soft mixtures made from cooked, grated mature coconut flesh and coconut water; cooked, pounded *taro* and coconut water, and small pieces of fish cooked by baking in the earth oven. If foods are not softened by grating and mixing with coconut water, it is customary to premasticate them for infants from nine to thirteen months of age. If foods other than *taro* (a very starchy root vegetable) are plentiful, infants ten to eleven months of age are given mashed ripe papaya, mashed ripe bananas, or mashed cooked *kumara* (sweet potato).

When teething occurs, infants are given pieces of cooked *taro* and the harder, mature coconut meat on which to chew. Breast feeding of a supplementary nature is continued until the child is 12 to 14 months of age when he is expected to begin consuming the usual adult diet.[1a]

Contemporary Infant Feeding

The majority of the infants today up to about nine months of age are breast-fed, whenever they cry. One infant was seen who had begun to take tea at the age of six months, and there were two chlldren 1 year of age who continued to be breast-fed at night when they cried, but who ate adult foods during the day. The vast majority of one-year old children had begun eating adult foods and drinking tea. Sugar was usually used in the tea, but milk was very seldom taken. Coffee grows wild on the island, and often the Maoris prepare and roast the beans for themselves, drinking it in place of tea, with coconut cream added. Only a few of the children between one and six years of age (and only four out of 24 between birth and the age of two years) receive dried milk to drink. The majority of families do not have enough money to buy dried whole milk, which is the only kind available in the trading stores, and they lack the motivation to do so. Cow's milk

and goat's milk are virtually unobtainable locally. When the children enter school at five to six years of age, some milk becomes available to them, since the government provides each child in school with a cup of reconstituted skimmed milk each day.

Some of the Maori mothers today do not like to breast-feed their infants. This is particularly true of the very young women, and the reason they give for this is that breast feeding keeps them confined to the home. There are some grounds for suspecting that it is really the husband who objects to breast feeding because he wants the woman to come with him to fish on the reef, work in the *taro* or *kumara* patch, tomato or orange plot. As a consequence of increasing contacts with Europeans, Rarotongan culture is changing from a subsistence economy to a money economy. There is much copying of the European methods of accumulating wealth. The wife is expected to help in the raising of tomatoes, citrus fruits, etc., although it is difficult for her to do this and to nurse a small infant as well.

Mothers begin introducing foods to their infants around four to five months of age, while breast feeding is still in effect. The time of introduction of supplementary foods seems largely an individual matter, and there is great variation in the amount of time and trouble a mother is willing to spend in preparing special foods for infant consumption. Some of these supplementary foods include papaya soup (made from green scraped papaya), root vegetables (*taro*, sweet potato, yam, and cassava), bananas and breadfruit in season, mashed and mixed with coconut cream. Bread that has been softened in tea is given at this age, too. Some infants receive only one or two of these foods, their diet being rather monotonous. No premasticated foods are given now.

From the age of six months to one year, these same foods are used, but their quantity is gradually increased. The only addition is that some protein food is given when the infant is about 10 months. Fish is the usual protein food, the available quantity depending on the father's fishing ability, the nearness to a reef opening, and the weather. Canned meat may be used, but eggs are almost never consumed by Maoris, and fresh meat (pork, poultry and goat) is reserved for festive occasions. Fresh fruits (papayas, mangoes, oranges, and guavas) are seldom prepared for infants; consumption of these foods begins when the children are capable of consuming them unaided. Beginning about the twelfth to the fourteenth month, infants are given some green vegetable a little more often. The only green leafy vegetable available to the majority of the Maoris is *rukau*, consisting of cooked young, tender leaves of *taro* plants chopped into small pieces, to which coconut cream is added as a sauce. Thorough cooking is extremely important in this particular dish since the leaves contain calcium oxalate salts which are very irritating to the mouth and gastrointestinal tract unless their stinging qualities are eliminated by prolonged heat application.

TABLE II

Mean Weights and Heights of Rarotongan Children*

Age	Mean wt. *lb*	No.	Range	Mean ht. *cm*	No.	Range
0–6 mo	15.0	3	12–17	—	—	—
6–12 mo	21.0	1	—	—	—	—
1–2 yr	23.0	13	12–32	75.8	5	66.8–82.7
2–3 yr	29.3	8	21–36	87.8	3	79.8–92.3
3–4 yr	35.8	9	27–44	96.3	8	92.4–102.3
4–5 yr	41.1	11	30–55	104.3	11	97.0–118.8
5–6 yr	42.5	20	32–48	109.8	20	99.0–119.7
6–7 yr	47.4	27	36–64	114.2	27	104.1–124.0

* The table combines male and female data.

When an infant reaches 12 to 14 months of age, he is treated as an adult with respect to his food intake. Little is done to see that he gets his proper share of the family food at meal times. Instead he competes with his brothers, sisters, and the adults in the family. On the whole, children learn quickly to find food for themselves and eat heartily whenever the opportunity arises. Some Europeans believe that the children eat a lot of food between meals, such as fruits and nuts which they pick up during the day. Or if they accompany any older persons to fish, they consume molluscs as they find them. Between-meal eating was actually observed and recorded far less frequently than was expected. Table I summarizes the ages for introduction of various foods commonly adhered to by Maori mothers at the present time.

In general, at meal time the head of the family is the first to get a share of the food, then follow the women and adolescents with the young children being served last. Usually there are sufficient staple foods (*taro*, *kumara*, banana, breadfruit, and cassava) to satisfy everyone, but the foods high in protein (fish, shellfish, or tinned meat) are so greatly es-

TABLE III

Wetzel Grid Evaluations of Rarotongan Children (Wetzel Grid for Infancy)

Channels	No. of children	Percentage
A_{12} to A_9 (obese)	3	4.1
A_9 to A_5 (stocky)	2	2.7
Total	5	6.8
(Wetzel Grid for Childhood)		
Above A_4 to A_2 (obese and stocky)	27	36.5
A_2 to M (stocky and good)	24	32.4
M to B_2 (good)	16	21.6
B_2 (fair)	2	2.7
Total	69	93.2
Grand Total	74	100.0

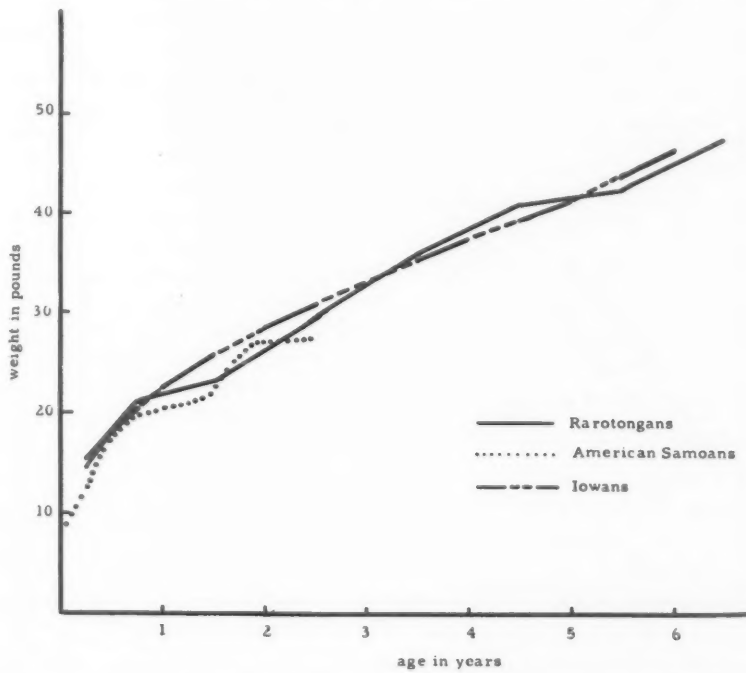

Fig. 1. Comparative curves of weight according to age of children on Rarotonga, American Samoa, and in Iowa, U.S.A.

teemed that it is unlikely that the infants and young children receive a proportionate share of them. The most common infant foods are those dishes made from coconut, papaya, or banana.

Growth and Development Data

The mean heights and weights of the Rarotongan children are presented in Table II. In Figures 1 and 2, these means are compared with the average heights and weights of American Samoan subjects[4] (birth to two years) and of Iowan children[5] (six months to six years). The Iowa data are used as representative of United States children as a whole, although it is realized that these children are from a relatively high status socio-economic group. The American Samoan study was done on the island of Tutuila, which has many features similar to Rarotonga. The most important of these for the present discussion being: (a) both are peopled by Polynesians, so the racial stock of the children that are compared is the same; (b) both are high volcanic islands, and therefore have very similar types of foods cultivated and available; and (c) the infant feeding practices and attitudes of Samoan mothers are almost identical with those of Rarotongan mothers.[4]

The 74 Maori children for whom there were both height and weight measurements were plotted on Wetzel grids.[6] Table III presents the results of this work; clearly the vast majority of Rarotongan infants and children are in the obese or stocky channels of the Wetzel grids.

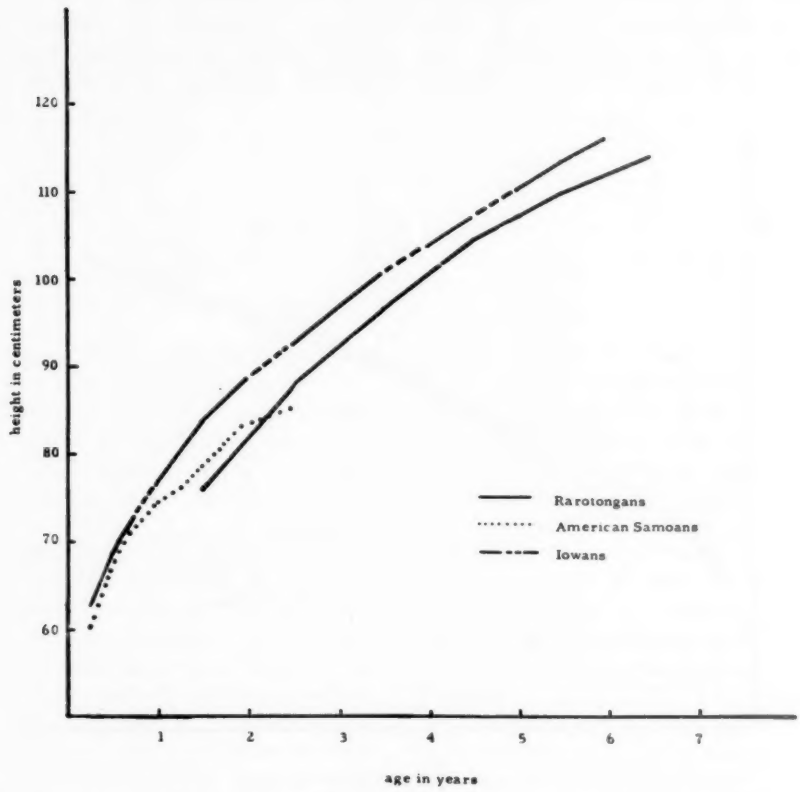

Fig. 2 Comparative curves of height according to age of children on Rarotonga, American Samoa, and in Iowa U.S.A.

TABLE IV

A Comparison of the Two Methods for Deriving the Caloric and Protein Intake of Rarotongan Children*

Calories

Age groups	Method no. 1 No.	Caloric needs	Coefficients per child	Mean intake	Range	Method no. 2 Mean percentage intake daily	Range
Birth–1 yr	9	1,208	0.40	1,507	790–3,226	124	65–267
1–3 yr	26	1,110	0.40	1,310	1,005–1,868	124	91–168
4–6 yr	32	1,480	0.50	1,911	1,292–4,591	129	87–310
	67						

Total Protein

Age groups	Method no. 1 No.	Recommended intake (g)	Coefficients per child	Mean intake (g)	Range	Method no. 2 Mean percentage intake daily	Range
Birth–1 yr	9	36	0.50	64	38–168	177	106–466
1–3 yr	26	40	0.60	58	26–117	144	65–292
4–6 yr	32	50	0.80	86	34–268	171	68–536
	67						

* Nutrient content of breast milk received by some of the children in the birth to 1 year group was not included. Needs in calories and protein were based on the recommendations of the Committee on Calorie Requirements[9] and the Food and Nutrition Board.[8]

Dietary Findings

Applying coefficients of consumption, the method recommended by Bigwood[7] and used in the presentation of the family dietary survey findings,[1a] the average daily intake of calories and protein by children under seven years of age was derived from the average daily intake of their families as a whole (Table IV). A second method was applied also, the percentage intake of calories and protein for each child. This was calculated by dividing the amount of these nutrients which he should have consumed from his family's average daily intake by the amount of calories and protein recommended for him.[8,9] As seen in Table IV, the mean percentage intake of both nutrients at all ages is above 100 per cent; however, the standard deviation indicates that there is wide dispersion of the individual values around the overall mean.

DISCUSSION

The size of the sample of Rarotongan children is small (100 subjects) as compared with the Iowa group and the American Samoa group (5,805 and 774 cases, respectively). On the basis of the data available, however, Rarotongan and American Samoan children appear lighter in weight from nine months to three years of age than do their American counterparts. This is the time when Maori children are weaned and begin competing with the older family members for a share in the family food supply. From three to nine months and from three to $6^1/_2$ years of age, the Rarotongan and Iowan children are more comparable in weight, the difference between the means not exceeding three pounds after the age of three years. Fry[3] reported that at 16 years of age both male and female Rarotongans were equal to, or greater in weight than, the Iowans, and that the Rarotongan heaviness was due principally to a preponderance of mesomorphy in adult males and females.

The Polynesian people are known to be one of the tallest races in the world, and they are a heavy people as well.[10] However, Rarotongan and American Samoan children, judged by the material presented in Figure 2, are not as tall as American children at any age below six

years. The greatest difference in stature appears to occur between birth and two and one-half years. It is unfortunate that there is no information on birth lengths and weights on Rarotonga, and the reason for this is that virtually all infants are born at home. In the absence of such information, extrapolation can be attempted, the results of which indicate that Maori infants are shorter at birth than United States children. It is known that Rarotongans of both sexes do not equal or exceed in height Iowans at any time through 18 years of age.[3]

Measurements on some 4,000 children in the north-central part of the United States were the basis for the compilation of the Wetzel grid; thus the grid, which is based on a cross-sectional study, and the stature and weight measurements on Iowa school children, which are from a longitudinal study, cannot be considered as standards of satisfactory growth for the racially different Polynesian children, but instead have been used for comparative purposes. There was a definite scarcity, only 2.7 per cent (2), of Rarotongan children in the "fair" grid channels, and none in the "borderline" and "poor" (B_3 and B_4) channels; the remaining 97.3 per cent (74) were in the "obese," "stocky," and "good" channels.

The author's belief that the majority of the Maori children are in these channels because of muscularity and not excessive subcutaneous fat is substantiated by the appearance and degree of activity of the subjects. It would seem that racial factors leading to the production of good musculature begin to exert their influence at an early age in Maoris. Environmental agents, such as the hardships involved in day-to-day living, probably contribute greatly to the development of mesomorphy which is necessary for successful participation in Rarotongan family and group work.

Because actual quantitative records of the food intake of individuals in a family were impossible to obtain, the amount of calories and protein that the children could reasonably have been expected to consume was calculated from the known amounts of these nutrients prepared for consumption by the entire family. As stated heretofore, young children compete with their siblings and the adults for a share of the food, and it is believed unlikely that children between one and two and one-half years receive their fair share. By the time they are two and one-half to three years of age, they have become adept at fending for themselves at meal times and receive more of all foods, the prestige foods as well as other types. Observations within homes and at feasts indicate that these are the generally-held habits and customs. Undue reliance, however, cannot be placed on the derived data presented in Table IV. Instead, such information should be interpreted as preliminary, and probably indicative of a trend, but nothing further.

If good musculature and good performance are accepted as the best criteria of adequacy, deficiencies of calories and protein would seem to be absent among young children on Rarotonga. Living in an environment with a mean annual temperature of 25° C (74.5° F), Maoris have a decreased physiologic demand for calories to be used in thermoregulation, in contrast with people living in more temperate areas, as in the United States. This factor was recognized in calculating the caloric needs included in Table IV. Another point of considerable importance is that there is a paucity of data on the nutritive content of many of the foods consumed on Pacific islands. It is very possible that some of these foods contribute in unknown but significant ways to the nutritional well-being of the natives. More knowledge of the efficiency of absorption and utilization of nutrients on a high fibrous diet would be of great benefit in assessing the nutritional status of Rarotongan children and adults.

It should be pointed out that Rarotongan children do not seem to have a high resistance to disease; skin lesions are particularly common and are believed to be related to improper habits of hygiene as well as nutritional status and tropical environment. No edema was seen in the young children, but this observation was based on a nonmedical appraisal, and it was not possible to obtain any serum protein determinations on blood samples.

Rarotongan infants are usually breast-fed longer than American infants and this provides the primary source of protein for a considerable period, since foods high in protein are intro-

duced late by United States standards. The protein that is obtained after breast feeding is discontinued, is primarily of vegetable origin; this until the children learn to obtain some of the fish and meat at the family table. Analysis of samples of breast milk from New Hebridean mothers,[11] has shown that the composition of their milk is only slightly different from that of Australian mothers. The lactose and calcium figures are inferior, although remaining within normal limits. Similar investigations of Cook Island mothers are needed.

In terms of protein and calories, it was likely that a good pregnancy and lactation diet was provided for the Rarotongan women included in the dietary survey. This can be seen by a consideration of the following data, particularly when it is borne in mind that the woman is second only to the male adults when distribution of the family food supply is made. The mean protein intake of the average family was found to be 693.4 g per day;[18] dividing the average number of persons per family (6.5) into the above figure yields 106.7 g protein/person/day for the average Rarotongan individual. In terms of the families' percentage intake of the recommended allowances of protein in the earlier report,[18] it was found that the mean percentage intake was 160.5 ± 79.2 per cent. Of the 41 families, only one household consumed less than 75 per cent of the recommended amount of protein, while six families had between 75 and 100 per cent of the recommended intake. The remaining 34 families consumed 100 per cent or better of their recommended protein intake. An examination of the tabular material presented in the earlier article on family food consumption made it evident that the adequacy of the mean caloric intake for the group and dispersion of families around the mean for the groups was almost identical with the protein intake data just presented.

Investigations carried out in the United States concerning the relationship between protein content of mothers' diets and birth lengths and weights of their infants have yielded conflicting results. The reports of Dieckmann,[12] Sontag,[13] Northrop,[14] and Ebbs[15] were similar in that no relationship was found. On the other hand, Burke[16] found a strong correlation between protein intake and length and weight of the baby; Wiehl[17] noted a moderately significant difference between birth length and weight of babies born to obese mothers who received vitamin and protein concentrates in addition to their regular diet, as compared with other obese mothers who did not receive either or both of these supplements.

It would seem that the postulated shortness at birth of Rarotongan infants as compared with American progeny, if it exists, could not be said conclusively to be the result of poor diet on the part of the mother. Neither the information on Rarotongans' food consumption nor the data available from current research would support so positive a statement.

It is impossible to know if Rarotongan children are realizing their full genetic potential for growth. Hooton[10] has accumulated evidence which points to the conclusion that stature is in the main of a hereditary character, although fluctuations in individuals and groups occur, within limits, through environmental causes (including unfavorable conditions of diet). Because he has described the Polynesians as one of the tallest races in the world, and since the data presented earlier indicated that Rarotongans never equaled the stature of Iowans through 18 years of age, some conception of the environmental factors besides diet is needed to properly assess the health status of Maori children.

Clinical Findings

Faine[18] reported from a survey in 1950 that of 365 Rarotongans of all ages, 53.4 per cent of the subjects were found to be Mantoux positive; the tests were made with 0.005 mg P.P.D. (Commonwealth Serum Laboratories, Australia) and the tests were read 48 hours later. Following the same procedure, 164 children between the ages of 5 and 16 years were tested by the author and the Assistant Medical Officer of the Cook Islands in 1953–54.[3] Positive Mantoux reactions were found in 82.6 per cent of the cases, 6.2 per cent of these were very strong reactions (4 plus on the usual scale). On clinical examination of the 164 Rarotongan school children some of the other findings in-

cluded:[3] (a) eye examinations showed the prevalence of conjunctival injection to be 95.7 per cent (swimming, diving, and the sun's glare were believed to have aggravated this condition); (b) skin infections were relatively common, being present in 26.1 per cent of the children, scabies accounting for 36 of the 42 cases; (c) pediculosis capitis was found on 7.6 per cent of the subjects and sepsis of the skin, including boils and yaws, was prevalent in 11.8 per cent; (d) general body scars of traumatic or infective origin were encountered in 97.5 per cent of the school children.

Faine[18] found that filariasis was an important endemic disease on Rarotonga, affecting males more frequently than females, and the prevalence among school children was 27.5 per cent, having increased by 11.2 per cent since a survey conducted three years previously. Overt manifestations of filariasis are common among the adult Maoris. Faine further reported the distribution of intestinal parasitic ova as follows: *Ascaris*, 57 per cent; *Trichuris*, 74 per cent; *Enterobius*, 4 per cent; *hookworm*, 38 per cent. It seems that once a child is old enough to move around, he becomes infected. No ova were found in any children under 1 year of age, but thereafter 87 to 100 per cent of the population (average 88 per cent) had ova present throughout the various age groups. Eosinophilia and hyperproteinemia were found to be common during childhood as well as adulthood; this was not considered surprising in view of the large amount of parasitic infection.

There have been no improvements with regard to environmental sanitation measures since the Faine survey, and their findings undoubtedly represent the present-day minimal status in filarial and helminthic infestations. The parasitic burden of individuals needs further investigation in order to determine the degree of its menace to health.

The developmental level of a child in terms of skeletal maturation is a consequence of environmental factors as well as heredity. In order to see if possible dietary inadequacies and numerous infections and infestations had had a deleterious influence on the skeletal growth of Rarotongan children, bone age quotients were calculated, after the determination of bone ages from wrist x-rays,[3] using the criteria of Greulich and Pyle.[19] The 160 Rarotongan school children (78 girls and 82 boys) on whom wrist x-rays were made were compared with a group of 45 American children (22 girls and 23 boys) selected at random.[20]

Student's "t" test was used to test the difference between the means of the groups and no significant difference was found between Rarotongan and American boys (94.90 ± 7.94 and 92.83 ± 13.80, respectively) or between Rarotongan and American girls (95.78 ± 7.63 and 92.49 ± 13.80, respectively); thus, it appears that the skeletal maturation of Rarotongan children proceeds no faster or slower than that of American children despite the prevalence of various infections. However, it must be borne in mind that the standards used to assess bone age were based on data from the United States.

SUMMARY

A study was made of the child-rearing customs and some aspects of the growth of Rarotongan children concurrently with a family nutritional survey. It was found that administrative programs to alter the care and feeding of infants and young children on Rarotongan have had no profound effects. Rather, the desire of the Maoris to emulate Europeans in order to become successful in business has led to some changes in the rearing of children. A need for further study of the influences of changing social and economic conditions on maternal and child health is indicated, as is the desirability of education for the preparation of suitable dishes from indigenous foods for young children.

The vast majority of children under one year of age are partly or entirely breast-fed. Weaning usually occurs in the first nine to twelve months, with the most common period for the introduction of solid foods into the children's diets being between four and five months. Protein foods of high biologic value are not often added to infants' diets until the tenth month of life. Judged from observations and records, general child care and feeding varied greatly with individual mothers, there appearing to be few rigid cultural rules.

The growth of Rarotongan children was compared with that of American and native Samoan children and it was seen that up to nine months of age, and from two and one-half to 6 and one-half years of age, the Rarotongans were more comparable in weight to Iowan children. The hazards of the weaning period and the sudden necessity to learn to fend for oneself at meal times are reflected in both the height and weight charts of children between nine months and two and one-half years of age. Maori children are not as tall as Iowan children at any age but appear to be more muscular than their American counterparts.

Clinical signs of malnutrition are very rare, but general morbidity and infant mortality are high. It is concluded, from the data presented on this small sample and on the basis of the presence of good musculature and good performance, that Rarotongan children probably have an adequate intake of protein and calories after the age of two and one-half years. It appears even more definite that the diets of Maori females during gestation and lactation contain adequate protein and calories.

The failure of Rarotongan children to be as tall or taller than American children is surprising, in view of the fact that Polynesians are traditionally described as one of the tallest races in the world. The possibility has been explored that the children fail to meet these expectations because of some unfavorable environmental factors other than diet.

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A Syndrome of Osteoporosis in Africans and Its Relationship to Scurvy

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IN RECENT years there have been many reports on idiopathic osteoporosis of the skeleton.[1–5] The condition affects women more often than men and usually occurs in elderly people but occasionally is found in young women after the induction of an artificial menopause. In this paper it will be shown that among Africans (South African Bantu) osteoporosis occurs in a younger age group and is more common in men than in women. In this community osteoporosis does not seem to be due to usually suggested causes and evidence is presented that it may be attributable to vitamin C deficiency.

MATERIAL AND METHODS OF STUDY

The subjects of this study were accustomed to a diet peculiar to most patients attending this hospital; it contains a high proportion of carbohydrate in the form of maize, and little animal protein and fat. It is usually adequate in calories and gross proteins.[6,7] For this study patients were selected whose x-rays of the spine showed crush fractures in association with osteoporosis and/or biconcave vertebral bodies, for which no obvious cause could be found. Cases with radiologic evidence of diminished bone density alone were excluded because of the difficulties of assessing minor variations of bone structure.

The role of vitamin C deficiency in the etiology of this syndrome was investigated in two ways; first, an attempt was made to ascertain whether osteoporosis and scurvy coexisted with greater frequency than could be ascribed to chance; secondly, a therapeutic trial with vitamin C was attempted.

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OBSERVATIONS

Age and Sex Distribution

During a period of one year all cases of osteoporosis encountered in this hospital were referred to us. Sixteen patients fulfilled the desired criteria and of these twelve were males, four females, and fourteen were under 60 years of age (Table I).

Clinical Features

Backache: Only two patients had no backache and the disease was revealed in the routine lateral radiographs of the spine. In 14 patients backache was the prominent symptom. In five the pain was of recent onset, the duration varying from 18 days to two months. These patients were bedridden and had extreme tenderness over one or more vertebral spines associated with spasm of the back muscles. Nine others had suffered from backache for many months or years and had become progressively more disabled. They showed a rounded rather than angular dorsal gibbus and all had lost height. Usually they could recall at least one episode of back pain which had necessitated bed rest for one or two months.

Hepatomegaly: Seven patients had firm, smooth enlargement of the liver extending two to four fingerbreadths below the costal margin. Liver biopsy revealed gross hemosiderosis in all, (Grade 3, Higginson *et al.*),[8] varying degrees of portal fibrosis in six, and gross monolobular cirrhosis in one.

Scurvy: Nine patients, when admitted to the hospital were suffering from classic acute

scurvy; three of these gave a history of previous acute attacks. The diagnosis was based on the finding of hot, brawny, tender swelling, occurring in typical sites in one or both legs.[9] In three patients biopsy of the swelling confirmed the presence of blood in the muscles and deeper layers of the skin.[9] Four patients also showed one or more of the following signs: perifollicular purpura, ecchymosis, subungual hemorrhages, hemarthrosis or spongy gums. Four of the eight were anemic (hemoglobin range 6.2–9.4 g/100 ml). In all the patients, bleeding time, coagulation time, blood platelet levels were within normal limits. The abnormal signs in all cases resolved within four to six weeks following intramuscular injections of ascorbic acid, 0.5 g daily. The remaining seven patients with osteoporosis, showed no evidence of acute scurvy on admission, nor did they show the stigmata of chronic scurvy, namely, tightly adherent skin encasing the ankles or an entire limb.[9] One patient, however, was suffering from a hemorrhagic effusion for which no cause could be found and which may have been a scorbutic "equivalent." This patient, who was admitted for acute backache, also had the signs of pericardial tamponade; aspiration revealed a hemorrhagic effusion and x-ray examination showed a moderately enlarged sac and thin parietal pericardium. The bleeding time, coagulation time, and blood platelet count were normal. After three aspirations at weekly intervals the effusion resolved completely. No evidence of tuberculosis was found in the pericardial fluid or elsewhere and 12 months later the heart appeared normal by clinical and radiologic standards.

TABLE I

Laboratory Data in 16 Cases of Osteoporosis

Age	Sex	Serum calcium *mg/100 ml*	Plasma phosphorus *mg/100 ml*	Alkaline phosphatase *King-Armstrong units*	Liver function tests				Serum proteins *g/100 ml*			E.S.R.* (Wintrobe)
					T.T.* *units*	T.F.*	C.R.*	T.A.*	Total	Albumin	Globulin	*mm/hr*
34	M	9.4	2.6	11.0	4.5	3+	3+	3+	7.0	3.0	4.0	5
41	M	10.2	3.8	8.6	3.3	—	3+	—	6.7	3.9	2.8	9
41	M	—	—	12.0	5.0	4+	4+	3+	7.0	2.4	4.6	3
43	M	9.6	3.5	8.0	—	—	—	—	7.3	3.5	3.8	7
47	M	9.9	4.0	7.0	—	—	—	—	7.6	3.2	4.4	42
48	M	10.9	3.8	5.9	—	—	—	—	7.7	4.2	3.5	3
50	M	10.0	3.5	11.0	4.0	—	4+	3+	7.5	3.4	4.1	20
56	M	9.0	3.0	11.5	—	—	—	—	6.9	2.7	4.2	37
57	M	8.0	3.1	10.2	6.0	4+	4+	3+	7.9	3.6	4.3	15
57	M	7.8	3.4	—	6.5	3+	3+	3+	8.0	3.0	5.0	—
60	M	9.4	3.5	—	—	—	—	—	7.3	3.8	3.5	31
67	M	9.5	3.4	—	4.0	4+	5+	3+	8.1	2.8	5.3	25
40	F	10.1	—	7.8	5.5	4+	4+	3+	8.3	3.0	5.3	36
40	F	9.8	4.0	10.0	7.0	3+	4+	3+	8.5	3.8	4.7	8
46	F	10.8	4.0	13.0	7.5	3+	5+	1+	8.8	4.5	4.3	9
50	F	9.5	3.0	13.0	4.5	4+	3+	3+	—	—	—	42

* T.T. = Thymol Turbidity; T.F. = Thymol Flocculation; C.R. = Colloidal Red Test; T.A. = Takata-Ara reaction (Ucko's modification). K.A. = King-Armstrong; E.S.R. = Erythrocyte sedimentation rate.

Negative Signs: Other conditions in which radiologic osteoporosis may be found, for example, endocrine disorders, metastatic deposits, steatorrhea, etc., were excluded by clinical and laboratory methods. One patient died of uremia due to pyemic abcesses of the kidneys, but the rest did not have renal disease. Two of the women were post-menopausal and two were menstruating normally.

Radiologic Findings

The entire skeleton was examined radiologically in 12 cases. Six showed well marked generalized osteoporosis affecting the ex-

tremities more than the skull. The lamina dura of the teeth, examined in six cases, was normal.

The Spine: Fourteen patients showed osteoporosis of the spine as judged by the following changes in the vertebral bodies, (1) generalized decalcification, (2) loss of detail in the spongiosa, (3) abnormal vertical striation (4) "cod fish" vertebrae. Fractures of one or several vertebral bodies were present in all

Fig 1. A compressed osteoporotic vertebrae is seen in the center of the roentgenogram.

cases. Collapsed vertebrae were of two types. In the dorsal spine they were indistinguishable from traumatic wedge fractures. In the lumbar region however, the osteoporotic vertebra became progressively compressed and appeared as a thin flat structure lying between two abnormally expanded intervertebral discs ("penny" vertebrae) (Fig. 1). Fractures were present in both dorsal and lumbar spines in six patients, in the lumbar spine alone in nine and in the dorsal spine alone in one.

Other Radiologic Findings: In four patients the lungs showed non-specific reticulation. In two of 13 cases examined the liver and spleen appeared abnormally dense; these appearances were probably due to hemosiderosis. In 13 cases examined there was no evidence of renal stone.

Laboratory Findings

The serum calcium level (Table I) in 14 cases ranged from 9.0 to 10.9 mg/100 ml; it was 8.0 and 7.8 mg respectively in the remaining two cases. The plasma phosphorus level was within normal limits. The erythrocyte sedimentation rate, as in Black's series,[3] was usually elevated despite the absence of fever, anemia or other obvious cause. Blood counts were normal except in four of the patients with acute scurvy. Sternal marrow smears in six cases examined showed numerous hemosiderin-laden macrophages but no other abnormalities. A flocculation test for syphilis (Eagle[10]) was positive in three of eight cases examined. Repeated examinations of the stool in five patients showed no excess of fat. Twenty-four-hour specimens of urine from three males aged 34, 41, and 50 years respectively, contained 12 to 16 mg of 17-ketosteroids and 10 to 12 mouse units of follicle-stimulating hormone, values considered to be within the normal range. In all patients examined the liver function tests were grossly abnormal, and the albumin-globulin ratio of the serum proteins was reversed (Table I). It is noteworthy that similar findings are frequently encountered in random African medical patients.[11]

Pathologic Findings

Two patients died. The first patient, a male, age 41, was admitted with hepatomegaly and signs of scurvy. Routine spinal x-ray examination revealed osteoporotic collapse of

the 5th, 7th and 8th thoracic vertebrae. There was no history of trauma. He died three weeks later from liver failure. Autopsy was performed by Dr. B. G. Grobbelaar and revealed advanced monolobular cirrhosis of the liver and marked hemosiderosis of the liver, spleen, pancreas and retro-peritoneal lymph nodes. The spine showed collapse of the 5th, 7th and 8th thoracic vertebrae. Histologic sections showed: (1) reduction in thickness of the bony corticalis enclosing the spongiosa; (2) attenuation and atrophy of the trabeculae; (3) numerous granules of hemosiderin in both free and fixed macrophages in the spongiosa; (4) no extracellular pigment and no evidence of the presence of osteoid tissue.

TABLE II

Incidence of Scurvy in 16 Cases of Osteoporosis Observed During a Period of 12 Months (August 1954–July, 1955)

	Number of cases	Incidence
Scurvy	11	69%
Classic acute scurvy on admission	9	
Scorbutic equivalent on admission	1	
Past history of scurvy only	1	
No scurvy, past or present	5	31%
Total	16	100%

The second patient was an elderly man known to have suffered from osteoporosis for at least two years. He developed acute scurvy one year before his death and from that time was treated with ascorbic acid and calcium. Autopsy performed by Dr. J. Higginson, revealed that death was due to a renal infection. The calf and thigh muscles showed deep brown staining due to hemosiderin deposition resulting from the previous scorbutic muscle hemorrhage. The liver, spleen and retroperitoneal lymph nodes and jejunum were grossly hemosiderotic. The spine showed collapse of many vertebrae and protrusion of the nucleus pulposus into the bodies. The changes were most marked in T8, 11 and L2 and 3. Sections of both normal and collapsed vertebrae, as in the first autopsied case, showed reduced thickness of the bony corticalis and attenuation and atrophy of the bony trabiculae. In addition, large areas of the spongiosa were replaced by fibrous tissue showing numerous iron-containing macrophages.

ASSOCIATION WITH SCURVY

Table II shows the incidence of scurvy in 16 cases of osteoporosis observed during a period of 12 months (August 1954 to July 1955). On admission nine patients were suffering from typical acute scurvy in some of whom a previous history of scurvy was elicited. One patient had a condition considered to be a scorbutic "equivalent" and one had experienced a previous attack of scurvy. Thus, 69 per cent of the osteoporotic patients were or had been scorbutic. In five (31 per cent), no evidence could be elicited of past or present scurvy.

TABLE III

Incidence of Osteoporosis in Scorbutics and Non-Scorbutics

	Number of cases	Incidence of Osteoporosis
Random non-scorbutics	150	0 (0.0%)
Classic acute scorbutics	48	9 (18.7%)

Table III shows the comparatively high incidence of osteoporosis (18.7 per cent) in a group of 48 typical acute scorbutics, as compared with a group of 150 random non-scorbutic subjects of the same age and sex, in which no instances of osteoporosis were found.

TABLE IV

Incidence of Scurvy and of Osteoporosis in Hospital Admissions

	Hospital total admissions	Number of cases	Percentage
Hospital incidence of scurvy August 1952–July 1953	30,760	40	0.13
Hospital incidence of osteoporosis August 1954–July 1955	26,650	16	0.06

Table IV shows that both scurvy and osteoporosis are uncommon diseases in this hospital, constituting 0.13 and 0.06 per cent of all admissions respectively, yet these two

relatively rare conditions were frequently found together in the same patient.

THERAPEUTIC TRIAL

Ten osteoporotic patients were divided into two treatment groups for long-term observation. Six received 500 mg of ascorbic acid by intramuscular injection daily. Four were treated orally with 3,000 I.U. daily of a vitamin D preparation (Radiostol, B.D.H.). Two of these failed to return for further study and could not be traced. In addition all patients received calcium gluconate 15 grams daily by mouth. Seven patients spent one to two months in the hospital and for the rest of the observation period subsisted on their usual home diet. One patient, treated with ascorbic acid, was deliberately kept in the hospital for a year and given a "full" diet.

Using a step-wedge as a radiologic standard, both groups were again x-rayed at intervals of approximately a month over a period of 9 to 15 months. Three untreated patients with osteoporosis whose records were available for the previous one to three years served as controls.

Results: Eleven patients, including the three controls, were observed for nine months to three years. Of these only one showed convincing radiologic evidence of recalcification and no worsening of the lesion. This patient not only received ascorbic acid but was kept in hospital for a year and had consumed a full mixed diet. Of the remaining ten patients, including the three untreated controls, all showed progressive deterioration as judged by further vertebral collapse, despite some evidence of healing of fractures in three.

DISCUSSION

The disease described here falls into the category of osteoporosis rather than osteomalacia, since histologic study reveals atrophy of bone and absence of osteoid tissue. Moreover, the values for serum calcium and plasma phosphorus were within normal limits, with two exceptions.

Two main theories are advanced to account for osteoporosis. On the one hand Albright and his school[12] consider it to be a disorder of osteoid tissue rather than of calcium-phosphorus metabolism. They maintain that endocrine imbalance or other factors, such as, deficiency of protein or of vitamin C, interfere with the production of osteoid tissue so that no new bone is laid down, while osteoclastic reabsorption of formed bone continues at the normal rate. On the other hand, there is experimental and clinical evidence that lack of calcium or phosphorus or of both may be responsible for osteoporosis.[1,4,13,14] It seems improbable that endocrine imbalance is responsible for the osteoporosis of Africans particularly in premenopausal women and middle-aged males with normal urinary steroid excretion. Lack of total protein seems an unlikely cause since the diet of Africans appears to contain adequate amounts of gross proteins. Nor can the abnormal pattern of the blood proteins be incriminated,[15] since similar values are frequently found in random African patients.

The calcium content of the diets of Africans is low and their serum calcium level is slightly lower than that of communities subsisting on higher calcium intakes. Walker and Arvidsson,[16,17] however, consider that these low serum calcium values do not predispose to poor mineralization of bone.

The findings of hemosiderosis in every one of the nine patients examined is a feature not encountered in other reported series of osteoporosis. Walker *et al.*[18] examined vertebrae obtained at autopsy from 77 Africans. All were siderotic, and 15 per cent contained more than 1 per cent of iron; but even in these severely siderotic vertebrae no correlation could be demonstrated between mineral density of vertebrae and their iron concentration. It is now well established that siderosis is a frequent incidental postmortem finding in Africans and that it increases in intensity with age.[19,20,21] Since osteoporosis appears to be a rare postmortem finding in the many Africans who suffer from hemosiderosis, it is therefore unlikely that a causal relationship exists between the two conditions. Furthermore, as far as we are aware there is no evidence in the literature that hemochromatosis causes osteoporosis.[22]

There is a wealth of experimental evidence to support the view that vitamin C is essential for the formation of osteoid tissue. Scorbutic animals do not form new bone and regularly develop osteoporosis.[23–25] In humans however the records are not quite so conclusive, although osteoporosis has been described in scorbutic children[26] and in soldiers dying of scurvy.[27]

The evidence linking osteoporosis with scurvy in this study is presented in Tables II, III and IV. The strongest argument in favor of a causal connection between the two is that such relatively rare conditions should be associated so frequently.

The therapeutic trial with ascorbic acid was inconclusive. Five of the six patients treated with ascorbic acid developed further vertebral collapse. Does this necessarily mean that ascorbic acid was ineffective? It may be inferred that a markedly osteoporotic skeleton has lost about 500 g of calcium[28]; it would therefore take several years to recalcify even on a high-calcium diet. Moreover, many of these African patients were obliged through economic circumstances to bear weight on their weakened spines and it is perhaps not surprising that they developed further collapse of vertebrae. The only patient who did not deteriorate and showed convincing evidence of recalcification of the spine was treated not only with ascorbic acid but had lived in the sheltered conditions of the hospital for a year and had eaten a full mixed diet. It is therefore impossible to assess what part ascorbic acid played in his improvement.

It remains to postulate how the episode of acute scurvy seen in the hospital can be held responsible for the established changes of osteoporosis and to explain why five patients in this series showed no signs of recent or past scurvy. It seems quite likely that Africans in this country suffer from acute or chronic scurvy without being aware of it. In a series of 47 consecutive cases of scurvy, five patients did not refer to their scorbutic signs. The disease may be mild showing itself merely by hemorrhage from an isolated site, such as the gums or muscles of one leg, without other evidence of a bleeding tendency.[9] The economic circumstances and the personality of the African are usually such that he is unlikely to stop working if he develops comparatively minor clinical signs, such as, bleeding gums or perifollicular purpura; he will not seek medical aid until a serious muscle hemorrhage or severe anemia drives him to a doctor. Not only is scurvy overlooked by patients, but in this hospital it is sometimes misdiagnosed as tropical myositis or thrombophlebitis; possibly it also masquerades in the form of idiopathic hemorrhagic effusions as in one case in this series.

It is conceivable, therefore, that these patients with osteoporosis may have suffered in the past from repeated minor attacks of scurvy or from mild chronic scurvy without being aware of it. Furthermore, it is assumed that all scorbutics, even those mildly affected, suffer from an abnormality of ground substance throughout the body, which also involves osteoid tissue.

CONCLUSION

In this African community many factors are present which singly or together may be responsible for osteoporosis. These are low dietary calcium, abnormal blood proteins, hemosiderosis and scurvy. These conditions, with the exception of scurvy however, are common to the majority of random African patients, among whom osteoporosis is rarely found. The association of scurvy and osteoporosis in this study is so striking that it amounts to presumptive evidence of a common cause. It is suggested that these osteoporotic patients may have suffered from chronic scurvy or minor attacks of acute scurvy without being incapacitated and that their chronic vitamin C-deficient state eventually led to osteoporosis.

SUMMARY

The clinical, radiologic and laboratory features of 16 cases of osteoporosis in Africans are described and postmortem findings in two cases are included. Nine patients were suffering from classic acute scurvy on admission and one from a possible scorbutic equivalent. A theory is propounded that chronic vitamin C deficiency may be responsible for osteoporosis

in this community. Among these patients there was a high incidence of hemosiderosis, portal fibrosis, disturbed liver function tests, and abnormal serum proteins. Reasons are given why these factors are not considered to be causally related to the osteoporosis.

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The Effect of Intrinsic Factor on the Absorption of Vitamin B_{12} in Older People

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VITAMIN B_{12} deficiency is known to exist in the absence of recognized clinical signs of primary pernicious anemia.[1] It has also been demonstrated that it may be associated with a lack of intrinsic factor. The simultaneous administration of vitamin B_{12} with intrinsic factor material has been advocated as a means of assuring absorption of vitamin B_{12} from the gastrointestinal tract, and of course has been used in the oral treatment of pernicious anemia.

This study was undertaken to determine (1) whether elderly people need added vitamin B_{12} in their diets and (2) the effect of exogenous intrinsic factor on the absorption of vitamin B_{12}. Two criteria were selected for estimating the absorption of this vitamin: urinary excretion measured by the Schilling test[2] and the plasma vitamin B_{12} level.[3,4]

METHODS AND MATERIALS

Choice of Subjects

Two hundred and one persons (76 females and 125 males), residents of the Marion County Home near Indianapolis, were selected for study. They had been admitted to this institution because of physical or mental illness or because they were unable to earn a living in the community. Their ages ranged from 37 to 92 years, the majority being over 50; the mean age was 69.3 years.

The diets at the Marion County Home were planned and prepared under the guidance of a trained dietitian. All subjects, prior to and during the test period, were offered a balanced diet daily.

Individuals were selected for absorption studies on the basis of the concentration of vitamin B_{12} in their plasma.[3,4] Of the total group of 201 people, 117 had plasma vitamin B_{12} levels of 0.5 mμg per ml or less and were used for further tests. Of these, 46 people had plasma vitamin B_{12} levels of 0.3 mμg per ml or below. Only 20 of the 46 subjects could cooperate enough to undergo tests for the estimation of intestinal absorption of vitamin $B_{12}Co^{60}$, with and without intrinsic factor, by the Schilling urinary excretion test.[2]

There were 71 people with plasma vitamin B_{12} levels of 0.3 to 0.5 mμg per ml and of these 40 were selected for studies in which plasma vitamin B_{12} levels were used as a criterion of absorption. They were divided into two groups with comparable individual and average plasma vitamin B_{12} values. One group of 20 then received oral vitamin B_{12} only and the other received intrinsic factor with vitamin B_{12}.

INTRINSIC FACTOR PREPARATION*

The intrinsic factor preparations used in these studies had been adequately standardized in patients with pernicious anemia in relapse and had been approved by the U.S.P. Antianemia Advisory Board. In the assay each patient received the intrinsic factor preparation with 15 μg of vitamin B_{12} orally for 36 consecutive days. All the anemic patients had an

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* Material supplied by Eli Lilly and Company.

adequate reticulocyte response and obtained complete remission. A 165 mg dose of preparation A represented 75 per cent of the amount of intrinsic factor which when combined with 15 μg of vitamin B_{12} had been shown to equal one oral U.S.P. unit of activity. The 50 mg dose of preparation B used in the plasma study was the amount of intrinsic factor which when combined with 15 μg of vitamin B_{12} had been shown to equal one oral U.S.P. unit of activity.

PLASMA DETERMINATION OF VITAMIN B_{12}

Since the same results in the assay for vitamin B_{12} were obtained with plasma as with serum, the greater yield of plasma per unit of blood made its use preferable. The vitamin B_{12}-plasma values were determined from a 20 ml sample of heparinized blood. All samples were centrifuged within two hours after being drawn. The plasma was refrigerated overnight and analyses begun the following morning. All the specimens were analyzed by an individual who had no knowledge of the age or health of the patient from whom the specimen was obtained. Plasma vitamin B_{12} concentrations were estimated by a microbiologic technic using *L. leichmannii* according to the U.S.P. procedure.[5] A modification was developed whereby the plasma samples could be assayed without clarification. Each individual's plasma value was based on an average of six separate determinations. Crystalline vitamin B_{12} at specific concentrations was used as the standard and analyzed each time the unknowns were assayed.

URINARY EXCRETION OF VITAMIN B_{12}

The method described by Schilling[2] was used to determine absorption of vitamin B_{12}, first, without exogenous intrinsic factor, and then with 165 mg (3/4 U.S.P. unit) of intrinsic factor preparation A. The amount of vitamin B_{12}-Co^{60} given was 3.36 mg (equivalent to 0.15 μc of Co^{60}) for each test. The radioactive vitamin B_{12} was administered in a capsule, as was the intrinsic factor. The patients were hospitalized in a special metabolic ward where administration of material and collection of urine was done by graduate nurses trained in metabolic procedures. Great care was taken to hydrate each patient in order to insure a good 24-hour urine collection. Unless this was done, reproducible results could not always be obtained.

After collecting the urine for 24 hours, the total volume was recorded and a 600 ml sample was removed. The urine was stirred for five min with a mixture of 1 g of Hy-Flo Supercel and 3 g of Magnesol. This slurry was then transferred to a sintered glass funnel and filtered using vacuum. This procedure was repeated on each urine filtrate to insure the removal of all the radioactive vitamin B_{12} present. The bottom of the funnel had been removed, and the underside of the sintered plate ground smooth. The funnels were placed on a 1 3/4" x 2" solid thallium-activated, sodium iodide crystal of a Baird-Atomic scintillation spectrometer instrument, and the recovered radioactivity was determined over the entire Co^{60} spectrum. A sample from each lot of the vitamin $B_{12}Co^{60}$ solution was used as a standard. The standard was prepared by adding 0.1 microcurie of vitamin $B_{12}Co^{60}$ to 600 ml of water and the mixture was taken through the above procedure. The counts obtained from this standard were increased by a factor of 1.5 for calculation. This standardization was done in order to correct for difference in geometric configuration of samples counted in capsule and funnel. The results were expressed in terms of the percentage of the dose of vitamin $B_{12}Co^{60}$ recovered in the urine. Each Schilling assay was performed twice, the second test being done after three to eight weeks of elapsed time. Before each procedure urine was collected overnight to check for the absence of vitamin $B_{12}Co^{60}$.

Patients on whom Schilling assays were done were subjected to gastric analysis. A fasting sample was obtained and the subject was given 50 mg of Histalog* subcutaneously.[6] Samples were then collected at 20-minute intervals for

TABLE I

The Range and Average Level of Vitamin B_{12} in Plasma of 201 People According to Age in Increments of 10 Years

Ages (yrs)	Number of subjects	Vitamin B_{12} mμg per ml of plasma	
		Range	Average
31–40	2	0.35–0.94	0.65
41–50	8	0.28–0.93	0.54
51–60	39	0.23–1.60	0.61
61–70	57	0.08–0.98	0.48
71–80	54	<0.06–0.93	0.45
81–90	40	<0.01–1.25	0.439
91–100	1	0.36–0.36	0.36

* "Histalog" (Betazole, Lilly).

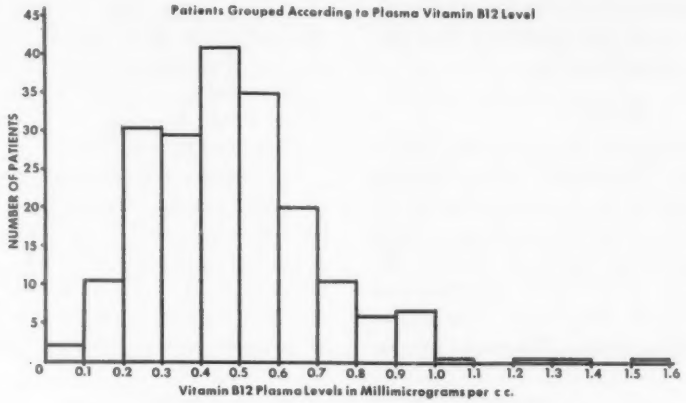

Fig. 1. Concentration of vitamin B_{12} in the plasma of 201 subjects.

one hour. The pH of the gastric juice was determined by means of a Beckman model H2 glass electrode pH meter. The patient was considered to have free acid in his gastric juice if any sample had a pH of less than 7.0.[7]

PLASMA VITAMIN B_{12} STUDY

Of the group of forty subjects with plasma vitamin B_{12} levels between 0.3 and 0.5 mμg per ml 18 individuals were given 5 μg of vitamin B_{12}, and 20 received 5 μg of vitamin B_{12} plus 25

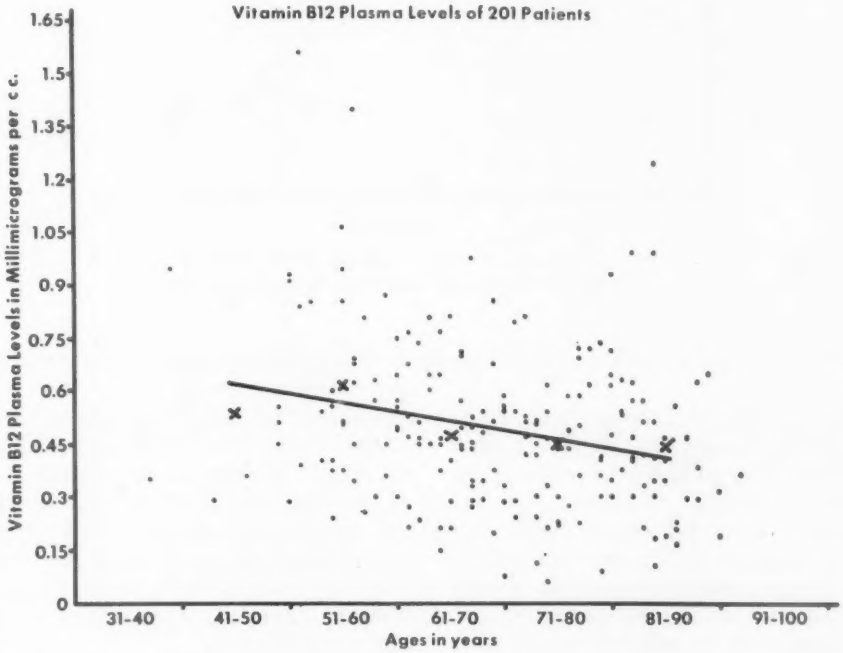

Fig. 2. Distribution of vitamin B_{12}, in mμg per ml, in the plasma of 201 subjects grouped according to age.

mg ($^1/_2$ U.S.P. unit) of intrinsic factor preparation B, twice daily for five months. Two subjects did not complete the study.

RESULTS

The plasma vitamin B_{12} level was determined on 201 subjects. Distribution of the plasma levels in relation to 0.1 mμg increments of plasma vitamins B_{12} is shown in Figure 1. The pattern was slightly skewed to the right. The general appearance of the curve, however, was compatible with the frequency distribution pattern of a random effect. The mean plasma vitamin B_{12} level in this series was 0.492 mμg per ml.

Figure 2 presents the distribution of plasma levels according to age. The range and mean plasma levels for age groups in 10 year intervals are shown in Table I. All subjects who had low plasma vitamin B_{12} concentrations (0.2 mμg per cc or less) were 64 years of age or older (Fig. 2). There were 45 patients with a plasma vitamin B_{12} level of 0.3 mμg per cc or less. Thirty-nine of these 45 subjects were 61 years of age or older. These data suggest a gradual decline in the plasma vitamin B_{12} levels with increasing age. This decline, calculated by the method of least squares, was 0.00521 mμg per ml of plasma per year of age. Statistical analysis indicates that the relationship shown above would be expected to occur by chance less than one time in 100.

The results obtained for the twenty subjects with plasma vitamin B_{12} levels of 0.3 mμg per ml or less that were studied by Schilling assay are shown in Table II. The first four subjects (G. B., J. G., E. S., and L. R.) had radioactive vitamin B_{12} uptakes in the same range as patients with pernicious anemia.[8] Subject E. S. suddenly became a markedly agitated paranoid-schizophrenic during the evaluation and on transfer to another institution was lost to the study. The other three men (G. B., J. G., and L. R.) with plasma vitamin B_{12} levels in the range usually seen in pernicious anemia, did not have the typical physical or hematologic findings characteristic of pernicious anemia. An examination by the staff neurologist, however, revealed abnormalities in sensory and motor function.

Case G. B. (Table II) was known to have had diabetes for 28 years. He had a loss of vi-

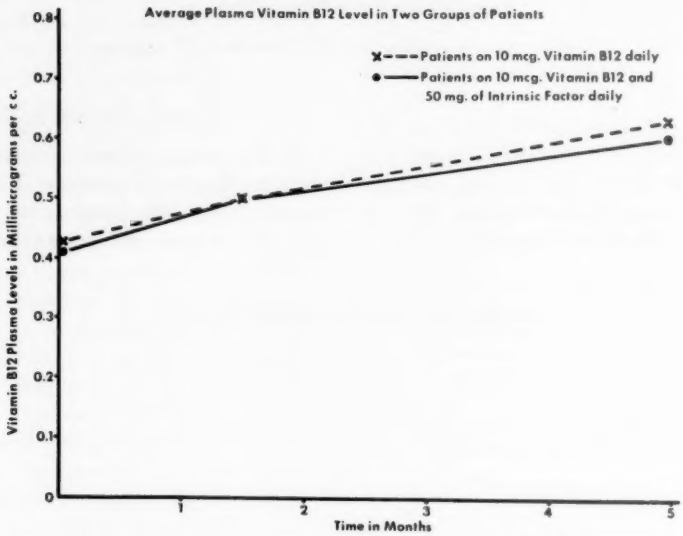

Fig. 3. Average vitamin B_{12} levels in the plasma of 18 people who received vitamin B_{12} alone and 20 subjects who received both vitamin B_{12} and intrinsic factor for five months.

bratory and position sense in his lower extremities. There was dysesthesia on the plantar surface of both feet. These findings were interpreted as peripheral neuritis rather than combined degeneration of the cord. No free hydrochloric acid was found in his gastric juice after Histalog stimulation. X-ray of the upper gastrointestinal tract revealed no abnormality. The hemoglobin was 88.6 per cent and the red blood cell count was 4.60 million per cu mm at the time the Schilling assay was performed.

J. G. (Table II)was known to have adenocarcinoma of the prostate and had been reported to have had a cerebral thrombosis two years previously. Neurologic examination revealed no evidence of motor or sensory changes that were typical of combined cord degeneration. No focal brain lesions could be demonstrated and the final diagnosis was "diffuse cerebrovascular disease and aging." The hemoglobin was 76.4%; red cell count was 4.60 million per cu mm. Roentgenogram of the stomach showed no abnormality. Acid phosphatase was 3 and alkaline phosphatase 10.1 King-Armstrong units.

L. R. (Table II) had been forced to give up his job and live in the Marion County Home because of difficulty in walking. A diagnosis of "multiple sclerosis" had been made in 1952, but examination by the neurologist during this study excluded this as a cause of present disability. At the time of the Schilling assay minimal evidence of cord involvement was observed. Changes in the left side were described as due to cerebral vascular disease. The red cell count was 4.68 million/cu mm; hemoblogin was 97.3 per cent. Gastric analysis after Histalog stimulation revealed no free acid in his gastric juice. X-ray of stomach showed no abnormality.

In the three subjects described above and

TABLE II

Effect of Exogenous Intrinsic Factor on the Urinary Excretion of Vitamin B_{12}

Patient	Age	Sex	Schilling assay: Vitamin B_{12} — Per cent B_{12} recovery	Schilling assay: Vitamin B_{12} and intrinsic factor — Per cent B_{12} recovery	Initial vitamin B_{12} plasma levels *mμg per ml*	pH of gastric juice
G. B.	74	M	0.46	8.95	<0.06	7.15
J. G.	84	M	0.88	3.20	<0.01	8.20
E. S.	54	M	1.30	7.38	0.23	Unknown
L. R.	70	M	1.36	7.29	0.08	7.90
J. S.	73	M	3.27	12.15	0.11	8.20
C. H.	64	M	4.04	4.60	0.20	Unknown
C. F.	77	M	4.32	5.96	0.22	1.00
D. D.	61	F	4.92	6.74	0.27	1.20
J. D.	62	M	5.08	8.80	0.24	7.20
L. T.	65	M	5.51	5.95	0.20	1.50
J. S.	76	M	6.36	6.90	0.27	5.80
E. L.	72	M	6.58	7.61	0.21	Unknown
J. R.	88	M	8.14	11.55	0.29	1.20
S. B.	71	F	8.57	7.72	0.23	1.80
M. W.	65	F	8.92	7.75	0.29	8.00
E. B.	83	F	9.05	8.10	0.20	1.30
E. W.	70	F	9.84	8.58	0.28	1.40
F. B.	67	M	9.90	12.28	0.27	1.05
C. M.	50	M	12.40	9.70	0.28	1.40
B. S.	72	M	14.50	14.40	0.29	1.40

Each subject received 3.36 μg of vitamin $B_{12}Co^{60}$ containing 0.15 μc of radioactivity. One dose of intrinsic factor contained 165 mg (75 per cent of 220 mg) of a standardized intrinsic factor preparation.

the fourth individual, E. S., a marked increase in absorption of vitamin B_{12} was accomplished by the simultaneous administration of intrinsic factor (Table II). A paired *t*-test applied to differences between the two treatments in these four people indicated that the differences were significant in that the results would not occur by chance 95% of the time.

In another subject (J. S.) (Table II) the per cent recovery of radioactive material from the urine was increased from 3.27 when vitamin B_{12} was given alone to 12.15 per cent when intrinsic factor was administered with the labeled cyanocobalamine. The concentration of vitamin B_{12} in the plasma of this patient was low, 0.11 mμg. He had no neurologic or hematologic changes. Gastric analysis after Histalog stimulation revealed no free acid in his gastric juice.

One individual (M. W.) (Table II) who had gastric juice of pH 8 exhibited no impairment of ability to absorb vitamin B_{12}, and the simultaneous administration of intrinsic factor did not produce a significant change in the percent of recovery of vitamin B_{12} in urine during Schilling assay in this subject.

Excluding the first four patients with extremely impaired absorption of vitamin B_{12}, the average urinary excretion of vitamin B_{12} was 8.67 per cent of the amount administered when given with intrinsic factor. In the same individuals the average vitamin B_{12} urinary excretion during Schilling assay when cyanocobalamine alone was given, was 7.59 per cent, Table II. Application of the paired *t*-test to individual patient differences showed that these results were not significantly different at the 5 per cent level. In short, of the 20 patients with low plasma levels (under 0.3 mμg/ml) four showed impaired absorption of vitamin B_{12} by the Schilling assay. Administration of intrinsic factor greatly increased the absorption of the vitamin in the four but not in the others.

The results, in the two groups of people, each with plasma vitamin B_{12} levels between 0.3 and 0.5 mμg per ml and who received vitamin B_{12} with and without intrinsic factor, orally, for five months are shown in Figure 3. Two people did not complete the study. Statistical analysis of the data indicates that the increase in plasma vitamin B_{12} for all 38 people at one and one-half months and five months was very highly significant at the probability level of 99.95 per cent. The difference in the rise of the plasma vitamin B_{12} between groups was not significant at the 95 per cent level of probability. In other words, in this group of subjects with moderately low plasma levels, intrinsic factor did not have any significant effect on the plasma level of vitamin B_{12} during supplementation over a prolonged period. However, oral vitamin B_{12}, with or without intrinsic factor, produced a statistically significant rise in plasma level.

DISCUSSION

These data indicate that at the age levels studied the plasma vitamin B_{12} concentration varies considerably from patient to patient. Similar variations have been observed by Boger and associates.[9] There is, however, a trend toward lower plasma concentrations of vitamin B_{12} with increasing age. This may mean that older people either eat a diet containing lesser amounts of vitamin B_{12}[10] or that they are unable to absorb adequate amounts of the ingested vitamin B_{12} because of a partial or complete lack of intrinsic factor. In Schilling assay studies Tauber and associates suggest the possibility of a decreased secretion of intrinsic factor.[11] Chow and associates have shown a lesser elevation of vitamin B_{12} blood level in older people than in young subjects following a standard oral dose of vitamin B_{12}. They concluded that older people cannot absorb vitamin B_{12} from the intestinal tract as well as the young. They also thought this was possibly due to lack of intrinsic factor.[12,13] Further evidence that old people have some decrease in the absorption of vitamin B_{12} has been obtained by Glass who states that, "The addition of a potent intrinsic factor preparation increased the hepatic uptake of radioactive vitamin B_{12} over 25 per cent in almost one-half of the cases in all age groups."[14,15]

In our studies those subjects who initially had a low vitamin B_{12} uptake (Table II) showed an increased absorption of radioactive vitamin B_{12} when intrinsic factor was given in addition to vitamin B_{12}.

In persons presumably having a defect in vi-

tamin B_{12} absorption associated with a lack of intrinsic factor, the concomitant use of a potent intrinsic factor preparation with vitamin B_{12} may avoid the development of neurologic changes that may occur in chronic vitamin B_{12} deficiencies.[16,17] This concept is particularly applicable to patients G. B., J. G., E. S., and L. R. They did not have the hematologic findings which ordinarily lead to a diagnosis of pernicious anemia.[8] Whether or not these neurologic changes are related to the vitamin B_{12} deficiency and could have been altered by the administration of vitamin B_{12} and intrinsic factor cannot be determined.

In the two groups of patients in which plasma vitamin B_{12} levels were used as an index of absorption, the parallel response obtained when vitamin B_{12} was given orally, with and without intrinsic factor, was expected. Both groups had vitamin B_{12} plasma levels in the low normal range at the beginning of the study and therefore presumably did not lack intrinsic factor. Similarly the subjects whose urinary excretion of vitamin $B_{12}Co^{60}$ was in the normal range were not expected to have a greater excretion of radioactive material when intrinsic factor was administered with the vitamin B_{12}.

The data also show definitely that the intrinsic factor preparations used in this study did not impair the absorption of vitamin B_{12}, after either acute or chronic administration.

SUMMARY

Determinations of the vitamin B_{12} level in the plasma were made on 201 persons between the ages of 37 and 92 years. A statistically significant decline in the plasma vitamin B_{12} level with age was found. This decline, calculated by the method of least squares, was 0.00521 mμg per ml of plasma per year of age.

Schilling assays were done on twenty elderly subjects. Administration of intrinsic factor increased the urinary excretion of radioactive vitamin B_{12} in those who had poor vitamin B_{12} absorption as well as low plasma levels. On the other hand, the subjects with a urinary excretion of vitamin $B_{12}Co^{60}$ in the normal range, but with low plasma levels, did not show a statistically significant change when intrinsic factor was given in addition to vitamin B_{12}.

Thirty-eight people with low normal plasma vitamin B_{12} levels (0.3 to 0.5 mμg per ml) were given vitamin B_{12} orally for five months. There was a statistically significant increase in plasma concentration of vitamin B_{12}. However, the increase in the amount of vitamin B_{12} in the plasma was just as great when intrinsic factor was given with vitamin B_{12} as when the subjects received vitamin B_{12} alone. No evidence for any inhibitory activity of the intrinsic preparations was found.

CONCLUSION

Low plasma levels of vitamin B_{12} were occasionally found among elderly people with no evidence of pernicious anemia. The oral administration of active intrinsic factor preparations enhanced the absorption of vitamin B_{12} in those subjects who showed impaired uptake by the Schilling test but had no significant effect if absorption was adequate. Prolonged administration of oral vitamin B_{12} raised plasma levels significantly.

ACKNOWLEDGMENTS

The authors wish to thank Mr. R. Morgan and his staff for their cooperation and help at the Marion County Home, Dr. C. N. Rice, Mr. J. L. Federman, and Mr. W. E. Baum for the processing and assay of the urines for the radioactive vitamin $B_{12}Co^{60}$, Mr. J. T. Stephenson and his associates for the microbiologic assay of vitamin B_{12} in the plasma, Dr. C. M. Gruber, Jr., and Dr. E. King for the statistical analysis of the data, and Dr. P. White for the neurologic examination of the first three patients. We also wish to express our appreciation to the nursing staff for their fine cooperation and especially to Miss V. Platz, R.N., Miss J. Clark, R.N., and Mrs. M. Thurman.

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Dr. A. J. Carlson and the Concept of Hunger

By FREDERICK HOELZEL*

THE DEATH of Dr. A. J. Carlson (Sept. 2, 1956) appears to have left his personal experience of hunger in the absence of gastric "hunger" contractions unpublished. In his published explanations,[1,2] Carlson, like Cannon, attributed hunger to the periodic "hunger" contractions of the fasting stomach and this explanation is usually referred to by others. However, in discussing the subject with me in 1917, Carlson revealed that, during a period in 1914 after a fast of about 5 days, he experienced unquestionable hunger with food in his stomach and therefore hunger without gastric "hunger" contractions. He felt certain that this was *hunger* and not the desire to eat which he regarded to be *appetite*. He said, however, that he was unable to explain this experience of hunger. Obviously, it was not explainable on the basis of his (and Cannon's) previously published concept of hunger. The lack of confirmatory and objective evidence at that time as to its being hunger and not appetite, presumably explains why Carlson did not report this observation when he reported the other findings concerning his five-day fast and the after-effects.[2,3]

However, he agreed that his experience of hunger independent of gastric "hunger" contractions would have been explainable on the basis of my concept of hunger. I believed that normal hunger was more or less directly related to the need of food[4] and that the nature of normal hunger was best indicated by the effect and after-effect of prolonged fasting. I had already fasted as long as 26 days in 1913 and my impression was that the reference of hunger to the stomach had decreased or tended to disappear after about the fifth day. I therefore thought that Carlson, by fasting only about five days, had not fasted long enough to note this. Carlson said that he believed that differences of opinion should be settled by experiment and I therefore volunteered to fast for about two weeks for a study of hunger to settle our differences.

To pursue this study I fasted 15 days in the summer of 1917, but observations on hunger and the fasting gastric motility and secretion were made daily for an additional eight weeks during which time I lived in Carlson's laboratory. The results failed to change our ideas about hunger. During a control week of observations before I began fasting, I was greatly impressed by the close correlation which usually existed between the recorded gastric "hunger" contractions and the desire to eat that was referable to the stomach. But it was obvious to me that this desire to eat was the "stomach craving" which in his book Fletcher[5] had designated as "false appetite," and which he had advised should be ignored because it did not reflect the need of food. That is, the desire to eat which I experienced when the gastric "hunger" contractions occurred in the morning could easily be ignored. During the afternoon, the desire to eat increased and became more and more imperative without a corresponding increase in the recorded "hunger" contractions. I was then following my usual previous practice of eating all of my food late in the day, or trying to wait for a normal appetite to develop before eating, as suggested by Fletcher. Filling the stomach once with food did not satisfy me, or left me still feeling hungry but without room for more food immediately. I practically always felt impelled to eat more food before I retired. In short, I then had the daily experience of hunger with food in the stomach and without "hunger" contractions as in Carlson's experience after his five-day fast, but the similarity of our experiences was not recognized then. Instead,

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Carlson considered my failure to be satisfied with a normal quantity of food to be evidence of bulimia.[4]

The observations made during my 15-day fast were regarded by Carlson as supporting his published concept of hunger. The periodic gastric "hunger" contractions and accompanying sensations were manifested throughout the fast.[4] The desire to eat was not as clearly related to the "hunger" contractions after the first few days as previously, but Carlson attributed the change in sensations to a depression of my appetite, as the recorded "hunger" contractions did not diminish. He previously explained a similar change in sensations during his five-day fast in the same way. According to my analysis however the change in sensations simply indicated that the desire to eat (hunger) was not directly related to the "hunger" contractions. My later studies also made it obvious that the use of an inflated balloon in the stomach to record the contractions had increased the gastric sensations and apparently also the "hunger" contractions, although they undoubtedly occur periodically throughout much more prolonged fasting.[6]

Observations made after the 15-day fast at Carlson's laboratory revealed some other discrepancies between the recorded gastric "hunger" contractions and the desire to eat. Some recorded "hunger" contractions were not felt while some epigastric hunger sensations were noted when no gastric "hunger" contractions were manifested. In fact, there seemed to be two or more types of epigastric hunger sensations and I believed that the keenest of these was produced by the acid gastric secretion. This was more clearly indicated in a later study.[7] However, there were times when the correspondence between the recorded "hunger" contractions and the desire to eat seemed to be perfect or normal and I realized that a more satisfactory explanation of hunger than that of Carlson and Cannon would have to take this apparently normal correlation into consideration.

In 1924, I found that the gastric "hunger" contractions occurred without any accompanying desire to eat when my stomach became empty after having eaten a very large amount of easily digested and rapidly absorbed food. In fact, by regulating the time and amount of eating, I found it possible to experience hunger with the stomach full of food in the morning, and satiety with periods of "hunger" contractions of the fasting stomach in the evening. Thus, a close dependence of the urge or desire to eat (hunger) upon at least some central (central nervous system or blood) need of food was clearly indicated. It consequently became obvious that my "bulimia" or previous tendency to overeat was due to my attempt to satisfy myself by stuffing my stomach instead of regulating my eating so as to satisfy central needs. Since then, I have found it much easier to avoid overeating or even reduce weight by eating most of my food relatively early in the day instead of late in the day or after some degree of fasting, as in 1917.

Carlson was satisfied with the evidence that the gastric "hunger" contractions could occur without being accompanied by any desire to eat. Actually, my finding only represented the result that might have been expected in making observations under more extreme conditions than those under which Carlson previously found that the desire or urge to eat was not as great during the first periods of "hunger" contractions following a meal as during subsequent periods.[2] My aim then was to report my findings by writing a book on hunger and appetite. Carlson offered to help me find a publisher if I did so. However, the manuscript I prepared was not regarded as satisfactory by Carlson. This and other considerations made it seem advisable that there should first be a study of some of the still unsolved problems associated with hunger. After publication of three reports of pertinent studies,[7–9] I prepared a report of my findings in 1924 and this was accepted by Carlson for publication without hesitation.[10]

Cannon, in a letter addressed to Carlson, complained about Carlson "allowing" the publication of this paper. Cannon thought that I failed to distinguish between hunger and appetite. In my opinion neither Cannon nor Carlson ever distinguished clearly between hunger and appetite. They never showed that the desire to eat, which they regarded to be appetite, was absent when the desire to eat,

which they considered to be hunger, was manifested. According to my view, there was only one kind of desire to eat and this varied in intensity and was or was not associated with gastric or other sensations. Carlson discussed the subject further with me before he replied to Cannon. Carlson still thought that he could distinguish between two drives or desires to eat and to this extent he continued to agree with Cannon. But to justify his sponsorship of the publication of my paper, he stated only that he did not believe that the publication of differing views should be prevented. With my approval, he sent along my written comments on Cannon's criticism which I had addressed to him (Carlson) while I happened to be away from the laboratory.

Carlson invited me to present my views or comments at two scientific meetings where hunger was discussed, but otherwise he referred only to his published explanations. However, he eventually had occasion to regret not having supported my concept of hunger more actively. This happened when his opinion was requested of a paper on hunger and appetite that had been submitted for publication in *Physiological Reviews* or the *Journal of Applied Physiology*. Carlson's explanation of hunger was severely criticized in this paper and there was no reference to my paper on central factors in hunger. Carlson was greatly upset because of the source of this paper. When he discussed it with me, I told him that he should have supported my view of hunger more actively. His only response to this was, "I know, I know." Carlson seemed to want to be credited at least with having recognized the value of my findings and conclusions. The paper was apparently rejected for publication in the form submitted because of Carlson's objections to it. I had expected my findings and conclusions to be confirmed by others in some ways much sooner as most of Carlson's associates and students who gave hunger special attention were not satisfied with his (and Cannon's) explanation of hunger and appetite.

Carlson and I agreed that hunger persisted throughout prolonged fasting and we published joint comments on that subject,[6] but I declined an invitation to join him in preparing a requested revision of Cannon's article on hunger and thirst for a new edition of the *Encyclopedia Britannica*.

Although Carlson did not publish a revision of the explanation of hunger published in 1916, the foregoing should make it clear that he did not rigidly adhere to his published views. Carlson certainly did not consider hunger to be simple gastric pain as implied by Janowitz and Grossman.[11] In nearly 40 years of association with Carlson, my impression always was that he regarded the essential element in hunger to be a keen desire, urge, or impulse to eat. Carlson's emphasis on the gastric sensations in hunger was obviously a consequence of using an inflated balloon in the stomach to obtain data on gastric motility. Although hunger can be experienced without gastric contractions and evidently even without a stomach, there seems to be no justification for a change in the definition of hunger such as Janowitz and Grossman suggested. They regarded the desire to eat to be appetite and based on learning, but evidence that the desire to eat is learned is lacking. I have indicated how the terms "hunger" and "appetite" can be applied to different factors affecting the food intake without the confusion involved in the explanations of Cannon and Carlson and without departing unjustifiably from their definitions.[12,13]

The discovery of Cannon's student, Washburn, and the independent discovery of Carlson that the common reference of hunger to the stomach is explainable by periodic contractions of the fasting stomach were significant contributions to our understanding of one factor that influences our food intake, but the inferences or speculations of Cannon and Carlson that were based on this discovery created a prolonged confusion. The more recent studies of others[14] have not helped very much to clarify the subject or to show how hunger and appetite can be controlled. An understanding of hunger and/or appetite depends partly on information obtained by introspection and there is need for more self-studies by investigators, such as those of Carlson and myself. Studies made on others, on infants or animals, largely yield only information "about it and about".

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Hereditary Factors in Protein Nutrition

By PAUL F. FENTON, PH.D*

EVIDENCE is accumulating that an individual inherits a characteristic metabolic pattern just as he inherits the color of skin, hair, and eyes. In our studies with highly inbred strains of mice, we have taken as our basic premise that an animal's genic make-up determines its endocrine balance which in turn establishes its metabolic pattern. Very likely all of our strains of mice make use of the same metabolic pathways. However, the degree to which each pathway is utilized will differ to an extent determined by the endocrine balance. Observations of differences in carbohydrate and fat metabolism among our strains of mice already have been reported.[1,2,3] One of the greatest differences observed so far lies in the response to diets containing 50 per cent fat.[4] Confronted with diets of such high caloric density, three of our mouse strains, C57BL/Fn, C3H/Fn, and A/Fn, consume enough extra calories to become obese at three months of age. Only one strain, the I/Fn, remains lean under these conditions.

CALORIES AND LOW-PROTEIN DIETS

Our four strains differ somewhat in growth rates when fed normal diets. However, when the protein content of the diet is reduced to 10 per cent, marked differences in growth are observed.[5] These may be explained on the basis of differences in voluntary food intake or on the basis of differences in efficiency of protein utilization. Both possibilities have been investigated.

Using diets containing only 5 per cent protein, we measured the efficiency of protein utilization for growth over a period of 20 days following weaning.[6] Voluntary food intake was markedly greater for A and C3H animals than it was for the I and C57 strains. However, the efficiency of protein utilization for growth was significantly greater only in the C3H strain. To eliminate differences in food intake, A and C3H mice were fed the 5 per cent protein diet in the amounts voluntarily consumed by I and C57 animals (approximately 43g). Under these conditions, the A and C3H mice lost weight at a 20-day food intake adequate to support significant weight gains in the C57 and I strains. When the 43 g of the 5 per cent protein diet were fed to C3H and A mice together with unlimited amounts of a nitrogen-free supplement, growth was again possible. This suggests that the C3H and A strains have a higher caloric requirement but not necessarily a higher protein requirement. The experiments indicate that there are real differences in metabolic pattern aside from the inherited differences in voluntary food intake.

PAIR-FEEDING

As a further test of this contention, we fed a 30 per cent protein-50 per cent fat diet to both

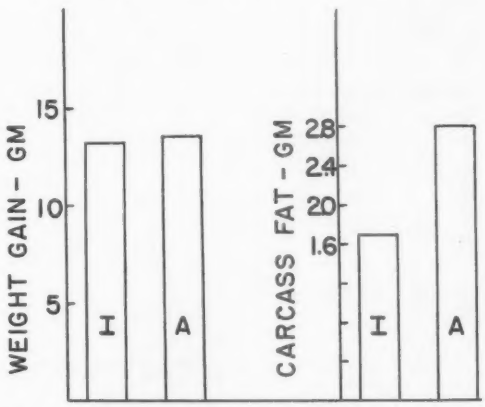

Fig. 1. Weight gain and fat deposition of two mouse strains under identical caloric intake.

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A and I strain mice. When fed *ad libitum*, this diet produces obesity in the A but not in the I strain. In the present experiment, however, mice of the two strains were carefully matched at weaning and then pair-fed for a period of 48 days. Average body weights of the two strains were virtually identical at the end of the feeding period. The I strain group, however, averaged 1.7 g of body fat while the A strain mice contained 2.8 g (Fig. 1). On the other hand, the nitrogen content of I strain mice was higher than that of the A group. Thus the A-strain mouse channels more of its available calories into fat depots and less into protein synthesis than does the I strain.

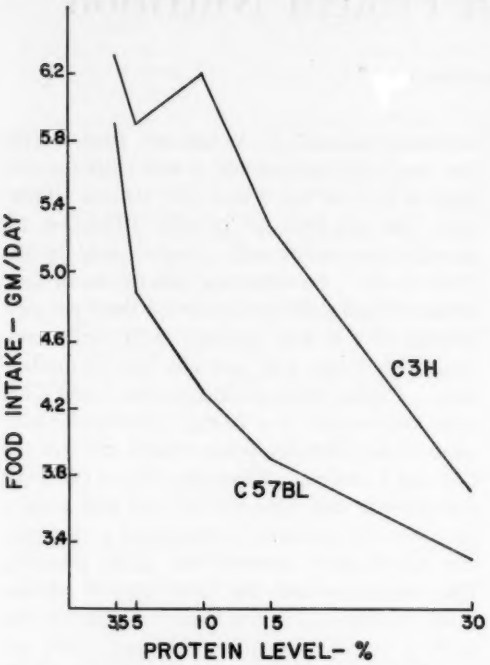

Fig. 2. Food intake at different dietary protein levels; 3.5 to 30 per cent.

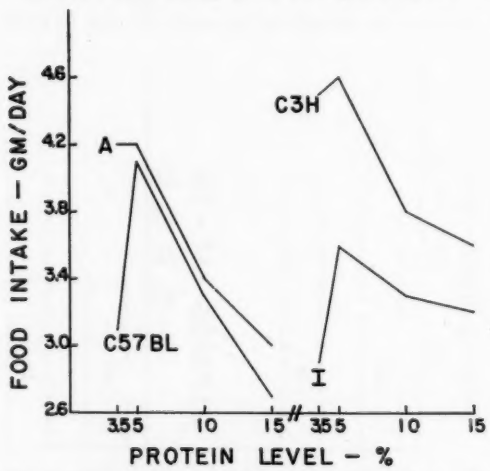

Fig. 3. Food intake at different dietary protein levels; 3.5 to 15 per cent.

PROTEIN LEVEL AND FOOD INTAKE

Experiments were also designed to look into the differences in food intake and, if possible, into the mechanisms underlying the differences. Brobeck and his associates[7] have suggested that food intake varies inversely with the protein level and thus with the specific dynamic action of the diet. A group of adult mice was fed a 30 per cent protein diet. Food intake was measured as soon as the body weight had stabilized. Thereafter the dietary protein level was dropped successively to 15, 10, 5, and 3.5 per cent. Food intake was greatest at the low protein levels and least with the 30 per cent protein diet (Fig. 2). In a second experiment the animals were stabilized on a 15 per cent protein diet. Later they received in succession the 10, 5, and 3.5 per cent protein diets. The mice were maintained at each protein level for considerable periods of time in contrast to the preceding experiment in which they were kept at each level for only one week. Again food intake increased as the protein level was lowered. However, when the 3.5 per cent level was reached, the food intake of C57 and I strain mice dropped sharply (Fig. 3). We suggest that this abrupt decrease in food intake is the result of a protein-deficiency state. If this is true, we have an indication that the C57 and I strain mice have a higher protein requirement than the A and C3H. This is supported by a nitrogen balance study[6] which showed the I strain to excrete more nitrogen than the A at several levels of nitrogen intake. In a further experiment the protein level of the diet was raised from 30 per cent to 50, 70, and finally 90 per cent. Food intake of I strain mice diminished with increasing protein level in accordance with Bro-

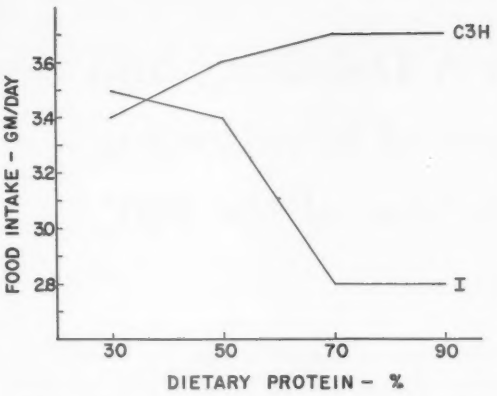

Fig. 4. Food intake at different dietary protein levels; 30 to 90 per cent.

beck's hypothesis. However, the C3H mice showed little change in food intake (Fig. 4). It must be remembered that the C3H mouse, as well as the A and to a certain degree the C57, exerts relatively poor control of its food intake.

GLUCOSE TOLERANCE

Glucose tolerance was determined in mice accustomed to different levels of dietary protein. Feeding a 90 per cent diet resulted in considerable elevation of the fasting blood sugar level. Otherwise the tolerance curve shows excellent utilization of glucose. The blood sugar levels observed in mice maintained on a 10 per cent protein diet were found to be generally lower than those of animals maintained on normal protein intakes. Glucose utilization, however, appeared not to be diminished. The data so far suggest that the effect of dietary protein level on food intake cannot be explained readily in terms of changes in glucose utilization.

GENETIC FACTORS

In our most recent experiments we have attempted to find out how metabolic patterns are inherited. Taking the A and the I strains which seemed to differ most drastically, we have started a series of crosses and backcrosses. Each line was tested by the following criteria: (1) rate of growth on a 10 per cent protein diet for 21 days after weaning, (2) endogenous N excretion, (3) weight gain on a 30 per cent protein-50 per cent fat diet, and (4) carcass composition after ten weeks on the high-fat diet. The results obtained so far indicate that each metabolic aspect studied is controlled by separate sets of multiple factors.

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Relation of Vitamin A Deficiency and Estrogen to Induction of Keratinizing Metaplasia in the Uterus of the Rat

By WALTER J. BO, PH.D.

IT IS WELL known that a deficiency of vitamin A and also overstimulation with estrogen causes a keratinizing metaplasia of the epithelium of the rat uterus. Wolbach and Howe[1] were the first to carry out detailed studies of the morphologic changes produced by the withdrawl of vitamin A from experimental animals. They observed that stratified squamous keratinizing metaplasia developed in all types of epithelia through the following sequence of histologic changes: atrophy of the original epithelium, proliferation of the basal cells which displaced the original epithelium and finally a differentiation into a stratified squamous keratinizing epithelium. In the rat the uterine changes were first observed to occur in the endometrial glands. Metaplasia of the epithelium of the uterus of the guinea pig is more marked than for the rat.[2] In vitamin A-deficient mice metaplasia of the uterine epithelium has not been observed to occur.[3]

Selye, Thompson, and Collip[4] were the first among many investigators[5–14] to observe that prolonged treatment with estrogen produces metaplasia of the epithelium of the uterus. Although all authors agree that metaplasia of the uterine epithelium can be induced in experimental animals by overstimulation with estrogen, there is no agreement about the manner of origin and development of the abnormal epithelium.

From the data available in the literature on keratinizing metaplasia of the epithelium of the rat uterus, it is not clear whether avitaminosis A exerts its influence directly on the epithelium independent of estrogen stimulation or whether it is dependent on estrogen for the induction of the keratinizing metaplasia. The experiments to be described in this paper were designed to provide information on the manner of origin and development of stratified squamous epithelium in the uterus of the rat by overstimulation with estrogen and to provide information on the relationship of avitaminosis A to estrogen in producing keratinizing metaplasia of the epithelium of the rat uterus.

MATERIALS AND METHODS

Three separate experiments were carried out to study the problems mentioned above. Rats of the Wistar strain were used in all the experiments. The animals were killed with ether and the uteri fixed for 12 to 24 hours in Zenker's or Helly's solution. Serial sections were made of each uterus and every tenth section was mounted and stained with Weigert's hematoxylin and eosin.

Specific information on the execution of the experiments along with the observations made will be presented under appropriate headings below.

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OBSERVATIONS

I. The Manner of Development of Squamous Metaplasia Induced by Estrogen[15]

Starting on the seventh day of age the rats were treated weekly with a single subcutaneous injection of 2 mg estradiol dipropionate.* Animals were autopsied every three days from the 3rd to the 27th day after receiving the first injection. Others were killed on the 33rd and the 39th day after initial injection with estrogen.

Uterine metaplasia was first evident in the animals autopsied on the 18th day after the first injection of estrogen, (Table I). Epithelial metaplasia was observed to begin as multiple foci which were located along the horns of the uterus, (Fig. 1a). The abnormal epithelium was formed by proliferation of the luminal epithelial cells. The foci of epithelial metaplasia grow by continual division, undermine the original epithelium and eventually separate the original epithelium from the underlying connective tissue. In advanced conditions keratinized epithelium was present, (Fig. 1b). Destruction of the luminal epithelium was not observed to precede the formation of squamous metaplasia.

TABLE I

Induction of Epithelial Metaplasia in the Rat Uterus by Weekly Administration of 2.0 mg Estradiol Dipropionate Beginning at Seven Days of Age

Number of animals	Days after 1st injection autopsied	Number of animals showing metaplasia	Extent of squamous metaplasia
25	3–15	0	–
5	18	4	+
5	21	4	+++
5	24	4	+++
5	27	4	++
5	33	2	+++
5	39	4	++

II. Influence of Ovariectomy on Vitamin A-Deficiency Induction of Epithelial Metaplasia[16]

Rats 20 to 22 days of age were divided into four groups. In group I the animals were kept intact and placed on a vitamin A-deficient diet.* The rates in group II were treated as those in group I except that they received a dietary supplement of vitamin A. The animals in group III were bilaterally ovariectomized and placed on a vitamin A-deficient diet. In group IV the rats were treated as in group III except that they received a dietary supplement of vitamin A. Animals were autopsied from the 8th to the 13th week of the experiment.

In order to determine whether the daily food intake of the vitamin-deficient animals was an important factor in producing symptoms of avitaminosis A rats of Group III and Group IV were pair-fed.

Metaplasia of the uterine epithelium of the vitamin A-deficient intact rats was similar to that previously reported,[1] (Figs. 2c, d, e). However, no metaplasia of the uterus was observed in the vitamin A-deficient rats following ovariectomy (Table II; Fig. 2).

TABLE II

Influence of Ovariectomy on Vitamin A Deficiency Induction of Epithelial Metaplasia in the Rat Uterus

Group	Number of animals	Intact or overiectomized	Vitamin A	Presence of squamous metaplasia
I	30	Intact	Deficient	Yes
II	10	Intact	Supplied	No
III	30	Ovariectomized	Deficient	No
IV	10	Ovariectomized	Supplied	No

The results indicate that the ovaries also have an important role in producing metaplasia in the uteri of vitamin A-deficient rats. Of the ovarian hormones, it is probably estrogen that is concerned with the metaplastic changes that occur in the uterine epithelium, since progesterone is primarily concerned with secretory activity of the epithelial cells whereas estrogen is primarily concerned with stimulating mitosis and cell growth.

Since the rats of group III in the pair-fed series showed external manifestations of vita-

* The estradiol dipropionate used in this study was supplied through the courtesy of the Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

* Vitamin A Test Diet U.S.P. XIV, General Biochemicals, Inc., Chagrin Falls, Ohio.

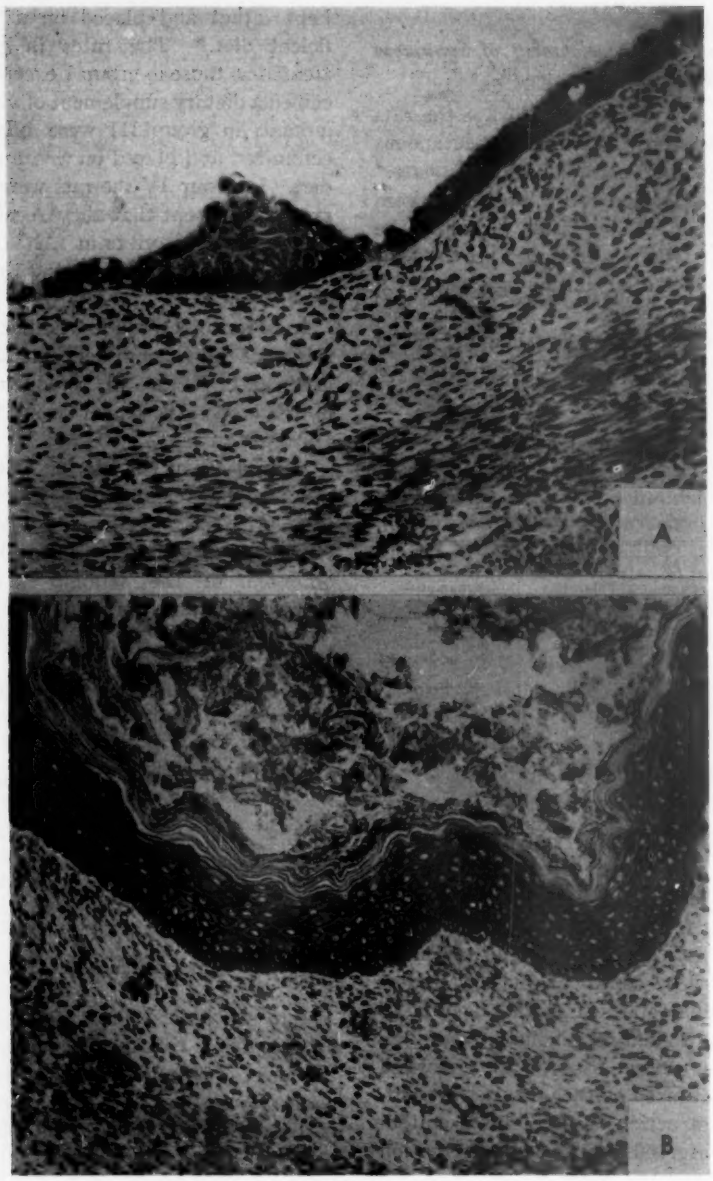

Fig. 1.

(a) Photomicrograph of a portion of the uterus showing the start of squamous keratinizing metaplasia following estrogen stimulation (hematoxylin and eosin) × 160. (b) Photomicrograph of a portion of the uterus showing extensive stratified squamous keratinizing epithelium following estrogen stimulation (giemsa stain) × 160.

min A deficiency and metaplasia of the lining epithelium of the trachea while the animals of group IV on the supplemented diet, which were pair-fed, exhibited no manifestations of vitamin A deficiency, it could be concluded that the changes observed were due to avitaminosis A and not to indirect effects of the deficiency.

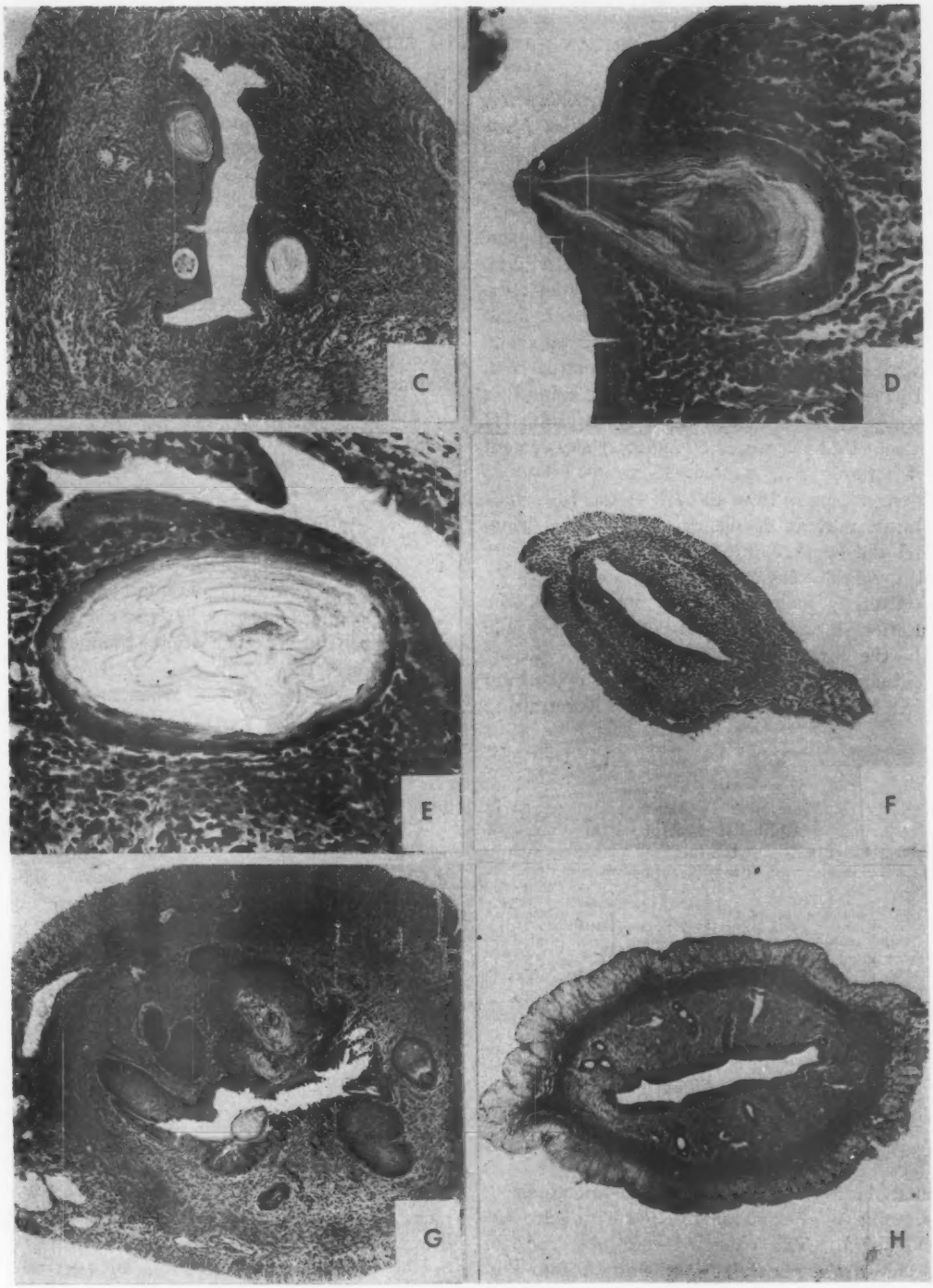

Fig. 2.

(c) Photomicrograph of a portion of the uterus of an intact vitamin A-deficient rat demonstrating stratification and keratinization of the glandular epithelium. The animal was autopsied during the 12th week of the deficiency (hematoxylin and eosin) × 70. (d) and (e). Photomicrograph of a portion of the endometrium of an intact vitamin A-deficient rat demonstrating extensive keratinization of the glandular epithelium. The animal was autopsied during the 12th week of the deficiency (hematoxylin and eosin) × 175. (f) Photomicrograph of the uterus of an ovariectomized vitamin A-deficient rat. No evidence of uterine metaplasia is present. The animal was autopsied during the 13th week of the deficiency (hematoxylin and eosin) × 55. (g) Photomicrograph of the uterus of an ovariectomized vitamin A-deficient animal treated with estrogen. Many foci of uterine metaplasia are demonstrated. The rat was autopsied during the 6th week of the experiment (hematoxylin and eosin) × 45. (h) Photomicrograph of the uterus of an ovariectomized animal on an adequate diet and treated with estrogen. No evidence of uterine metaplasia. The animal was autopsied during the 9th week of the experiment (hematoxylin and eosin) × 30.

III. Relation of Vitamin A Deficiency and Estrogen in Production of Epithelial Metaplasia[17]

Rats 20 to 22 days of age were divided into four groups. In group I the animals were kept intact while the rats in group II were bilaterally ovariectomized and all the animals were placed on the vitamin A-free diet mentioned heretofor. In group III the animals were bilaterally ovariectomized, maintained on a vitamin A-deficient diet and treated with 1 μg estrogen every third day. The animals in group IV were treated as those in group III except that they received a dietary supplement of vitamin A. Animals in group I and II were autopsied from the 7th to the 13th week of the vitamin deficiency while rats of group III and IV were autopsied from the 5th to the 10th week of the experiment.

Uterine metaplasia was present in the uteri of intact vitamin A-deficient rats while in the ovariectomized vitamin A-deficient animals metaplasia of the uterine epithelium was not observed (Table III). Keratinizing metaplasia occurred in the ovariectomized vitamin A-deficient rats treated with estrogen (Fig. 2g). The changes were observed to occur in the glandular epithelium before the lining epithelium. Uterine metaplasia was not present in the ovariectomized animals on an adequate diet and also treated with estrogen (Fig. 2h).

TABLE III

Relation of Vitamin A Deficiency and Estrogen in Production of Epithelial Metaplasia in Uterus of the Rat

Group	Number of animals	Intact or ovariectomized	Vitamin A	Estrogen	Presence of squamous metaplasia
I	15	Intact	Deficient	No	Yes
II	15	Ovariectomized	Deficient	No	No
III	30	Ovariectomized	Deficient	Yes	Yes
IV	30	Ovariectomized	Supplied	Yes	No

DISCUSSION

The observations made in the present study demonstrate that keratinizing metaplasia induced by estrogen begins as multiple foci which are located along the uterine horns. These foci of epithelial cells extend toward the lumen of the uterus and also laterally from point of origin to undermine the original luminal epithelium. The superficial cells of this new cell growth become keratinized. By this process the entire luminal epithelium is replaced by a keratinizing epithelium.

The origin of epithelial metaplasia produced by estrogen stimulation differs from the metaplasia which occurs in vitamin A deficiency in that in the estrogen-induced the change takes origin in the luminal epithelium while in that following nutritional deficiency the changes originate in the endometrail glands. The epithelial metaplasia in the rat uterus produced by estrogen stimulation was more pronounced than that produced by avitaminosis A.

It has been suggested by other investigators that squamous keratinizing metaplasia of the uterus results from a local vitamin A deficiency regardless of any other factors.[18] The results obtained from the present investigations do not support that conclusion. If all keratinizing metaplasia is due to a local vitamin A deficiency regardless of any other factors, then such changes would be present in the uteri of ovariectomized vitamin A-deficient rats. The observations made in the present studies demonstrate rather clearly that uterine metaplasia following avitaminosis A occurs only when the epithelial cells are under the influence of estrogen. The synergistic action of vitamin A deficiency and estrogen in producing uterine metaplasia is evident by the pronounced metaplastic changes observed in the ovariectomized rats on a vitamin A-deficient diet and treated with estrogen as compared to the absence of changes in the ovariectomized animals on a vitamin A free diet or in the ovariectomized rats on an adequate diet treated with estrogen.

No definite relationship exists between vitamin A deficiency and estrogen in producing abnormal cornification of the vagina. The

change occurs in the intact as well as in the ovariectomized vitamin A-deficient rats.[19–21] It has been reported that cornification of the vagina following estrogen treatment is altered by excess vitamin A.[22,23] Recently, tissue culture technics have been used to study this relationship between vitamin A and estrogen in producing keratinized epithelium. The vagina has primarily been used for this study. It has been demonstrated that estrogen can produce cornification of the mouse vaginal epithelium *in vitro*.[24] Also, *in vitro*, keratinization of the rat vagina was observed to take place in cultures that contained a standard medium.[25] The keratinization that occurred was probably due to a lack of available vitamin A. The uterus, up to the present time, has not been used for *in vitro* studies. However, if such studies were undertaken interesting observations would be made on this problem of the relationship between vitamin A deficiency and estrogen in producing keratinizing metaplasia in the uterus of the rat.

These observations indicate that the abnormal growth that occurs in the uterus and that which has been reported to occur in the vagina following avitaminosis A cannot be considered to be the same. Although the end result, a keratinized epithelium, is the same the cytological processes involved in producing the change are different in the two organs. In the vagina the abnormal growth is more of a hyperplastic change and, as mentioned above, occurs in the intact and ovariectomized rat while in the uterus the growth is a true metaplasia and occurs only in the intact animal. This difference in response of the uterus and vagina to vitamin A deficiency may result from the difference in the embryology, morphology and physiology of the two organs. The conclusions drawn from observations made on the vagina in avitaminosis A or between vitamin A and estrogen cannot be generalized to include the uterus.

The question which arises in regard to keratinized epithelium is which of the two causes, estrogen or vitamin A deficiency, is the primary factor in producing the change. On the basis of the present work it can be concluded that vitamin A deficiency *per se* cannot be considered to be the primary factor in inducing keratinizing metaplasia in the uterus of the rat. Estrogen seems to have an equal role in producing the change. On the other hand, from the experimental data that are available on the rat vagina, vitamin A deficiency seems to be the primary factor in producing abnormal cornification.

Although vitamin A supresses the cornification of the vagina induced by estrogen, it cannot be definitely concluded that vitamin A plays a general role in the prevention of all keratin formation. In the epidermis of the male rat, topically applied vitamin A dissolved in sesame oil did not interfere with the keratinization process.[26] Likewise, in the guinea pig, vitamin A dissolved in oleic acid, linoleic acid or alcohol did not inhibit the formation of the stratum corneum of the skin.[27] Also, vitamin A did not prevent the estrogen-induced hyperkeratosis of the nipple epidermis in the guinea pig.[26]

The mode of action of vitamin A in maintaining normal uterine epithelium is not clear. Since vitamin A has not been demonstrated by fluorescence microscopy in epithelia that are known to undergo keratinization in depleted animals, it has been suggested that vitamin A *per se* is not responsible for maintaining normal epithelia but a metabolite of vitamin A may be.[28] It seems that in order to maintain the integrity of the uterine epithelia a balance exists between vitamin A and estrogen and when this balance is disrupted a keratinizing metaplasia occurs.

SUMMARY

Metaplasia of the uterine epithelium of estrogen-treated rats begins as many independent centers that grow and coalesce to produce a keratinized stratified squamous epithelium which replaces the original uterine epithelium.

The origin of epithelial metaplasia produced by estrogen stimulation differs from the metaplasia which occurs in vitamin A deficiency in that in the former the change takes origin in the luminal epithelium and the latter in the endometrial glands. The epithelium produced by estrogen stimulation is thicker and more

heavily keratinized than that produced by vitamin A deficiency.

Keratinizing metaplasia in the uterus of the rat was observed to occur only in intact animals on a vitamin A-deficient diet or in the ovariectomized, vitamin A-deficient rats treated with estrogen. The results demonstrate that estrogen has an important role in producing keratinized epithelium in avitaminosis A and the change cannot be considered to be due to only a local vitamin A deficiency.

From the present investigation it can be concluded that vitamin A deficiency is not the primary factor in producing keratinizing metaplasia in the uterus of the rat since estrogen plays a role in producing the change.

The mode of action of vitamin A in maintaining normal uterine epithelium is not known, but it seems that a balance may exist between estrogen and vitamin A in order to maintain the integrity of the uterine epithelium and when this is disrupted keratinizing metaplasia occurs.

The abnormal cornification of the vagina that occurs in vitamin A deficiency of the rat was compared with the uterine changes and it was concluded that the two are not the same. In the vagina the change is more of a hyperplastic change while in the uterus it is a true metaplasia. Therefore, the conclusions drawn from the observations made on the vagina in avitaminosis A and between vitamin A and estrogen cannot be generalized to include the uterus.

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This Journal Receives Honor Award

We are pleased to announce that THE AMERICAN JOURNAL OF CLINICAL NUTRITION has been selected as the recipient of the 1957 Honor Award for Distinguished Service in Medical Journalism presented by the American Medical Writers' Association at its annual meeting in St. Louis, September 27–28, 1957.

This award is made for "accuracy, clarity, conciseness, and newness of information in articles, editorials, and other material; for excellence of design, printing, and illustrations, and for distinguished service to the medical profession, rendered by United States and Canadian medical periodicals."

Among the medical journals previously so honored are *The American Journal of Medicine* and *The American Journal of Surgery*, also publications of The Yorke Publishing Co.

To the American Medical Writers' Association and to our editors, abstracters, and especially to our contributors, go the deep gratitude of the Editor and Publisher.

Editorial

Diet and Atherosclerosis—the Evidence from Israel

Those who read the journals on nutrition and biochemistry as well as laymen reading news weeklies have found universal acclaim for the theory of the dietary origin of atherosclerosis during the past year. The readers of the *Lancet* have had presented to them a remarkable series of articles and letters dealing with the effects of diet on blood coagulation, blood lipids and coronary disease, as well as some reiterating the older view that atherosclerosis is due solely to wear and tear on the arterial wall and is unrelated to diet or plasma lipid.[1]

It is now just 50 years since Ignatowski first produced experimental atherosclerosis by feeding rabbits milk or eggs. Long before this a relation of coronary disease to living conditions was apparent, and Osler taught his students that the disease spared the poor but attacked men "who eat, drink and smoke too much." Today the student of medicine may be taught by authorities of high repute that atherosclerosis is unrelated to diet and that coronary attacks should be treated by diets based on eggs, milk, custard and ice-cream; or that the disease is due to "obesity and gluttony," with no special food being considered harmful aside from its calorie content.

The enormous literature on experimental atherosclerosis, brought about by dietary manipulation with cholesterol and fat supplements, and on regional and social variations in coronary disease, blood cholesterol, and the dietary content of animal fat, is dismissed as irrelevant by many experienced cardiologists to whom each year hundreds of patients with coronary disease turn for advice. A recent 90-page monograph on heart disease summed up the evidence on smoking and coronary disease in two sentences, that on diet and coronary disease in three pages. But yet the reviewer for the *Journal of the American Medical Association*, passing over everything else in the book, cited the essayist's acceptance of the view given by Osler and now supported by such overwhelming evidence, and warned that "many other cardiologists disagree with him." It is unlikely that the conservatives will be impressed even by the data on coronary disease, plasma lipids, and dietary customs among the immigrants to Israel.[2,3]

The Yemenite Jews lived apart from their Arab neighbors and from world Jewry for nearly 2,000 years, speaking Biblical Hebrew and adhering to a diet based on bread, vegetables, and vegetable oils. Settled in Israel, recent immigrants from Yemen adhere to this way of life, and fat (mostly olive oil or seed oils) provides less than 18 per cent of their caloric intake. In men aged 55 to 60 years the blood cholesterol level averages less than 160 mg per 100 ml; and the death rate from all arteriosclerotic diseases is below five per 10,000. However, male Yemenites who have lived in Israel and Palestine for 20 years or more have less restricted diets, with 21 per cent of calories derived from fat. They use some dairy products. Their cholesterol levels at the same age average 200 mg per 100 ml. Deaths due to arteriosclerosis are 33 per 10,000. The European Jewish immigrants have blood cholesterol levels over 240 mg per 100 ml and 86 per 10,000 die of arteriosclerosis each year. Their diets, cholesterol levels, and death rates are similar to related groups in urban United States communities.

While undoubtedly there are individual and familial differences, and perhaps even racial differences, in the effects of various diets on blood cholesterol, as well as differences in the incidence of clinical coronary disease at any

given age in men or women with similar elevations in cholesterol (or beta lipoprotein, or S_f 10-200) levels, the important fact remains that in any population of Whites or Negroes, Mongoloids or Semitics, the average level of blood cholesterol and the incidence of coronary occlusion rises with any increase in the average daily intake of animal fat, and especially of butter fat.

Substituting corn oil for butter in New York[4] or in Sweden,[5] regularly lowers blood cholesterol; safflower oil is equally effective, but neither Ahrens,[4] nor Malmros[1] found it actually more effective. Cottonseed oil has a comparable effect, but olive oil permits a slight rise from the level achieved with the other oils. No fat commonly eaten in large amounts causes so marked a rise as butter fat, and no communities have higher blood cholesterol levels or coronary death rates than those with liberal intakes of butter fat.

This year, in the many celebrations of the Harvey Tercentary, frequent references have been made to the stupid way in which most leading physicians opposed the theory of the circulation. When we recall that Harvey lived long before the dawn of the scientific era, that his contemporaries were not impressed by experiments on embryos and snakes, that the practice of medicine and surgery was not affected by assuming a circulatory rather than a tidal flow from the heart, and that no confirmatory evidence was produced for years after Harvey's demonstrations, we can pardon his contemporaries. But how will the medical historian of the year 2207 regard the reaction of some segments of the medical profession in the last half century to the vast and concordant evidence for the dietary basis of atherosclerosis?

—WILLIAM DOCK, M.D.

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Diet Therapy

Adapting Therapeutic Diets to Jewish Food Customs

By MILDRED KAUFMAN, M.S.*

THE FOOD habits of Jewish people living in the United States today differ with each individual, depending on his degree of acculturation and whether he belongs to the Orthodox, Conservative, or Reform group. With the days of immigration thirty or more years behind them, the food selection of American Jewish families is now influenced to varying degrees by the eating pattern of the country in which they live, the food habits of the country from which they or their forefathers came, and the Biblical and rabbinical regulations concerning food known as the Jewish dietary laws. The Jewish individual whose eating habits are similar to those of the general population poses few unusual problems to the non-Jewish physician, dietitian or nurse when dietary guidance is necessary. It, therefore, is sometimes puzzling to these professional people when they must work with another Jewish patient whose food selection is restricted by the rules of the religion which he observes.

Variations in observance are due largely to the differences in interpretation and importance placed on the dietary laws by the three schools of thought among American Jews today. Orthodox Jews still place great value on the traditional and ceremonial practices of their religion, and observe the dietary laws under all conditions. Reform Jews place much less emphasis on rules which they consider to be purely ceremonial and tend to minimize the significance of dietary laws. Conservative Jews stand between these two groups and, while nominally adhering to dietary laws, sometimes draw the distinction between the observance of the rules in the home and outside.

It is helpful for anyone working with Jewish patients to know the basic elements of their dietary laws, and the significance of these laws to the observant Jew. It is also helpful to know some of the favorite foods and food customs related to everyday living and to special holidays.

THE DIETARY LAWS

The dietary laws are Biblical ordinances codified and interpreted by the rabbis in the Talmud into specific instructions concerning those foods which are fit and proper for the Jewish people to eat. Regulations include selection, preparation and service of the foods involved. The Bible gives no reason for these rules, but observant Jews feel that the rules known as Kashruth and hallowed since the time of Moses, are a positive means of self-purification and of service to their God. Although many hygienic and ethical bases have been alleged for these rules, the spiritual factors of sanctification and self-discipline are the primary motivations for those who adhere to them.

Rules pertain chiefly to the selection, slaughter and preparation of meat. Animals allowed

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for food are those quadrupeds with a cloven hoof who chew a cud, specifically cattle, sheep, goats and deer.[1,2] Permissible fowls are chicken, turkey, goose, pheasant and duck.[3] All animals must be inspected for disease and slaughtered by a ritual slaughterer (Schochet) according to specified rules which provide for minimum pain to the animal and maximum draining of blood in the slaughtering. With the quadrupeds, only the forequarter of the animal may be used. Only if the hip sinew of the thigh vein can be removed is the hind permissible.[4] Beef, veal, lamb, liver, chicken and turkey, freshly killed, according to ritual, are available to Jewish housewives at special kosher butcher shops and are more expensive than the same meats would be in the regular markets. Since only the forequarter of the animal is used, many of the cuts are the less tender ones and the choicer steaks, chops and roasts are not available from the kosher butcher shop.

Mosaic law also repeatedly forbids blood as food, since blood is synonymous with life.[5–8] This necessitates the traditional process of "koshering" the meat and poultry to remove all blood before it may be cooked. This is a process of soaking the meat in water, salting it thoroughly, allowing it to drain and then washing it three times to remove the salt. (This process probably removes from the meat some of its iron and B-complex vitamin value too).

From another oft-repeated statement in the Bible, "Thou shalt not seethe a kid in its mother's milk,"[9–11] has come the rule against combining meat and milk in the same meal. Milk or milk foods may be eaten immediately before the meat, but not with it. After meat has been consumed, six hours must elapse before milk products may be used. Also, because of this rule, traditional orthodox Jewish homes must keep two completely separate sets of dishes, silver, and cooking equipment, one for "fleischig" (or meat) meals and one for "milchig" (or dairy) meals.

The fish prescribed in the Bible are those with fins and scales.[12,13] Shellfish and eels are therefore excluded. Fish may be eaten with either dairy or meat meals. Since rules pertaining to fish are less strict than those relating to meat, fish is commonly used by orthodox Jews to enable them to adhere to the dietary laws when they must eat away from home.

Eggs, too, may be used with either meat or with milk. However, any egg yolk containing a speck of blood may not be used, since the blood spot is considered the sign of a new life.

Fruit, vegetables, cereal products and all of the other foods that make up a normal nutritious diet, may be used without restrictions. Canned or frozen foods, bakery products, crackers, confections, prepared food mixtures and margarine, until recently, were viewed skeptically by orthodox Jews because of doubt as to possible sources of ingredients, combinations of ingredients and conditions of manufacture. At the present time, there are an increasing number of food manufacturing companies preparing these foods under acceptable kosher standards to satisfy the most observant.

TYPICAL MEAL PATTERN

Within the restrictions of the dietary laws, the basic foods recommended for good nutrition can be used in sufficient quantity. A meal pattern which would fit both the dietary rules and the requirements of a nutritionally adequate diet would be:

MEAL PATTERN	TYPICAL MENU
Breakfast	
Fruit, citrus—1 serving	Orange juice
Cereal, whole grain or enriched—1/2 cup	Oatmeal with milk and sugar
Milk and sugar for cereal	
Egg—one	Soft cooked egg
Whole grain or enriched bread—1 slice	Toast
Butter—2 teaspoons	Sweet butter
Beverage	Coffee with cream, sugar
Luncheon (or Supper)	
Cheese, egg or fish—1 serving	Noodle pudding*
	Cottage cheese and sour cream
Vegetable, green or yellow, raw—1 serving	Chopped raw vegetables
Bread, whole grain or enriched—1 slice	Pumpernickel—sweet butter
Butter—2 teaspoons	
Dessert	Applesauce
Milk—1 cup	Milk

	Dinner
Soup	Borscht
Meat—3 oz	Pot roast of beef
Potato—1 serving	Potato pancake
Vegetable—1 serving	Peas and carrots
Whole grain or enriched bread—1 slice	Lettuce and tomato Pumpernickel bread
Fruit	Dried fruit compote
Beverage	Tea with lemon

* Noodles baked with egg, seasoning and sometimes cottage cheese and sour cream.

MODIFICATIONS FOR THERAPEUTIC DIETS

It is possible to provide a nutritionally adequate normal diet within the restrictions of the Jewish dietary laws (Table I). The next question is how to adapt this basic diet for the various therapeutic diets.

When a restricted caloric intake is required, the basic meal pattern can easily be altered according to the usual principles of caloric restriction. It should be noted that many Jewish housewives use chicken fat generously in preparation of meat meals and the caloric value of this ingredient in their cooking must be brought to their attention. Many Jewish patients eat bread, noodles, dried legumes, coffee cakes and other pastries in quantity and these too must be restricted to reduce caloric intake. When explaining caloric restriction to Jewish patients, emphasis should be put on increased use of raw fruits and raw low-calorie vegetables as important parts of the diet.

Diabetic diets, as well as low-calorie diets, can be planned to provide variety by the use of Exchange Lists prepared by the American Dietetic Association, American Diabetes Association, Inc., and U. S. Public Health Service.[14]

When developing a meal plan for the Jewish patient, the need for taking a careful dietary history cannot be sufficiently stressed. For

TABLE I

Nutritive Value of Basic Diet Pattern*

Food	Measure	Weight *g*	Calories *g*	Protein *g*	Fat *g*	Carbohydrate *g*	Ca *mg*	Fe *mg*	A IU	Ascorbic acid *mg*	Vitamins Thiamine *mg*	Riboflavin *mg*	Niacin *mg*
Milk or equivalent	2 cups	488	335	17	19	24	576	0.4	780	6	0.18	0.84	0.6
Meat or fowl†	3 oz (raw wt.)	75 Cooked	210	18	15	—	10	2.8‡	4,600	—	0.09‡	0.56‡	5.0*
Egg	1	54	75	6	6	—	26	1.3	550	—	0.05	0.14	Tr.
Other protein§	1 serving	60	105	11	9	—	107	0.6	235	—	0.03	0.71	1.0
Whole grain or enriched cereal	½ cup (dry)	20	75	2	Tr.	16	8	0.6	—	—	0.11	0.03	0.7
Whole grain or enriched bread	4 slices	100	275	9	3	52	79	1.8	—	—	0.24	0.15	2.2
Potato	1 medium	150	125	3	Tr.	29	17	1.0	30	21	0.14	0.05	1.5
Green or yellow vegetable	1–2 servings	150	45	3	Tr.	9	67	1.5	4,690	35	0.12	0.12	0.9
Other vegetables	1 serving	100	35	1	Tr.	7	19	0.6	660	15	0.06	0.06	0.6
Citrus fruit	1 serving	100	45	1	Tr.	12	27	0.4	120	47	0.07	0.03	0.2
Other fruit	2 servings	200	125	1	1	32	24	1.0	1,200	18	0.08	0.08	0.8
Butter	4 teaspoons	20	145	Tr.	16	Tr.	Tr.	—	660	—	Tr.	—	Tr.
			1,595‖	72	69	181	960	12.0‖	13,525	142	1.17‖	2.77	13.5‖
Recommended dietary allowances¶													
Women (25 years)			2,300	55	—	—	800	12	5,000	70	1.2	1.4	12
Men (25 years)			2,300	55	—	—	800	12	5,000	75	1.6	1.6	16

* Food values are based on "Composition of Foods—Raw, Processed, Prepared," by B. K. Watt and A. L. Merrill, Agriculture Handbook, No. 8, Bureau of Human Nutrition and Home Economics, Washington, D. C., 1950. Calories and vitamin A have been rounded off to the nearest 5 and protein, fat, carbohydrate to the nearest whole gram.

† This assumes the use of beef, veal, or lamb, five times a week, chicken one time during the week, and liver one time during the week.

‡ Although no data are available, it would seem that there would be some loss of these nutrients due to the koshering process, and values would probably be somewhat below those used here.

§ Average of protein foods used at the non-meat lunch or supper, includes cheese, egg and fish.

‖ Calorie needs are met by using more of the basic foods, and by adding desserts, sugar, cooking fat, etc., as desired. If part of these added foods include whole grain or enriched breads and cereals, the iron, thiamine and niacin content will be increased.

¶ *Recommended Dietary Allowances*, 1953, National Research Council, Washington, D. C.

those patients observing the dietary laws, the meal plan can easily be made to include the milk allowance with breakfast and the one "dairy" meal. The other meal planned as a meat meal should avoid use of milk products. Interpretation of "Meat Exchanges" to include egg, cheese and fish for the "dairy" meal must be carefully stated. The patient will also need help with "Fat Exchanges" to show him how he may use butter, sweet or sour cream and cream cheese with the "dairy" meals, and some chicken fat with the meat meal. Vegetable shortening, vegetable margarine, oil or salad dressing and nuts can be used with either.

Many patients will appreciate the thoughtfulness of the physician or dietitian who shows him how to fit some of his favorite foods into the Exchange Lists. For example, when it is not necessary to restrict sodium intake lox or herring may be used as Meat Exchanges; and appropriate servings of kasha, bagel or matzoh may be used as Bread Exchanges. A descriptive list at the end of this article defines some of the foods that Jewish patients often ask to have included in their diets.

Special thought is also required for the diabetic on fast days, particularly the Day of Atonement, "Yom Kippur." For the mild diabetic, controlled by diet alone, fasting may be feasible. The more severe diabetic who requires insulin yet wishes to fast should be encouraged by his physician to discuss his problem with his rabbi in order to be convinced of the importance of continuing his regular pattern of eating even on this holiday.

Jewish patients who require sodium-restricted diets often have difficulty in adjusting to the regimen. For those who observe the practice of koshering meat at home, as previously described, there is the conflict of whether to use the meat without this salting process, or to modify the salting process hoping to remove the added salt more completely. It was found that meat koshered by the usual process, and then boiled, contained about 334 mg of sodium/100 g portion. A similarly koshered piece of meat cooked by broiling contained 375 mg of sodium. However, it was found that the sodium content could be reduced to about 63 mg of sodium/100 g portion of meat by the following process. First, it is lightly salted and allowed to stand with the salt for the religiously permissible minimum time, then it is rinsed and soaked in water; finally it is boiled in a generous amount of water and the broth discarded.[15] Another practice which might be acceptable to some patients is to use crystalline ammonium chloride instead of sodium chloride for the koshering process.[16]

Many of the favorite foods of the Jewish people are highly salted. Salted fish like herring and lox, kosher style corned beef and other smoked and salted meats and fishes, pickles and pickled green tomatoes are but a few of the foods which are frequently enjoyed at family meals. However, unsalted or sweet butter is preferred by many families and this, as well as dry, unsalted cottage cheese, is easily available in food stores in Jewish neighborhoods. Unsalted matzoh, usually used for Passover, but available throughout the year are also acceptable as a cracker or bread substitute for the sodium-restricted diet.

Bland diets used for patients with peptic ulcer offer no problems in the initial stages when protein is supplied by milk, cheese and eggs. Changes in texture and consistency can be made in the usual manner. When meat is added to the diet, the meat meal must again be planned without the creamed foods, milk desserts and beverages which are commonly included with this type of diet. Plans for in-between meal snacks should also recognize the six hours which must elapse between consumption of meat and milk. Extra milk between meals can usually be placed in the mid-morning and between a dairy luncheon and a meat supper. In many cases, milk at bedtime will also be acceptable. If not, an egg or meat sandwich might be suggested.

The above discussion states some of the most important considerations to be kept in mind in planning the more usual therapeutic diets with orthodox Jewish patients. Principles here stated can be applied to the needs of individual patients for any other type of diet which might be prescribed. For these patients, every effort should be made to fit

the therapeutic diet into the religious dietary laws. When there is true conflict between the principles of the diet and the religious regulations, the patient should be encouraged to discuss the problem with his rabbi to consider effecting a practical compromise. This is usually possible when the patient is convinced that the physician or dietitian understands his problem and is trying sympathetically to work it out with him. Actually orthodox law permits, even requires, the breaking of dietary laws when it is a matter of life or death. However, many patients are genuinely upset at the thought of breaking the dietary laws in any way, even during illness.

FOOD CUSTOMS RELATED TO HOLIDAY OBSERVANCE

Consideration of the food habits of Jewish people must necessarily include brief mention of some of the dietary aspects of the more important holidays. Most important of the holy days is the Sabbath or day of rest observed on Saturday. The meal on Sabbath eve or Friday evening is the choicest of the week and usually includes both fish and chicken. On the Sabbath itself, no food is cooked or heated, so all food eaten is cooked the previous day and either kept warm in the oven or eaten cold.

Festival holidays of Rosh Hashanah, the New Year in September, Succoth, the Fall harvest holiday, Chanukah, the feast of lights in midwinter and Purim, a gay holiday in spring, have associated delicacies which may be used or avoided according to dietary needs.

Yom Kippur, or the Day of Atonement, occurs ten days after Rosh Hashanah and is a day of fasting when there is abstinence from all food and drink, including water, from sundown on the eve of the holiday to sundown on the holiday. People who are ill and pregnant women are urged to refrain from fasting. As mentioned heretofore where the patient persists in his desire to fast he should be advised to consult his rabbi.

Dietary consideration must especially be given to Passover, a Spring commemorative festival lasting eight days. During this period, no leavened bread or cake may be used. Matzoh, an unleavened bread, is eaten and all cake and baked products are made from flour of ground up matzoh or potato starch, leavened only with beaten egg whites. For low-calorie or diabetic diets, three-fourths of a square or round matzoh is equal in carbohydrate value to one slice of bread.[17] No salt is added to these traditional Passover matzoh. In planning diets with patients, it should be noted that many of the favorite Passover dishes used are variations of fried matzoh or matzoh meal pancakes and are prepared with generous amounts of fat.

In the celebration of the Sabbath and the festivals, it is customary in Jewish homes to serve sweet grape wine as part of the religious observance. This wine is about 13 per cent alcohol and 17 per cent sugar.[18] Usually only about a 3 oz glass is served except at the Passover ceremonial dinners (Seders) when it is part of the ritual to fill the wine glasses four times. If at all possible, it is helpful to the patient to show him how he may adjust his diet to include this wine for holiday celebrations.

FOOD TERMS

The Jewish people have many favorite foods which they have learned to enjoy in the many countries of the world in which they have lived. Recipes for these foods have been adapted to fit the dietary laws, but otherwise closely resemble similar dishes prepared by the nationality groups who originated them. For consideration of these foods for possible inclusion in the patient's prescribed diet, the list of definitions of these foods is given.

Bagel (Baigel)—A doughnut shaped hard yeast roll.

Blintzes—Very thin rolled pancakes usually filled with sweetened cottage cheese mixture and served with sour cream; may also be filled with ground beef mixture or fruit mixture.

Bob—Fava beans served as salted nuts.

Borscht (Borsch)—Sweet and sour soup made either with a meat stock and beaten egg or made without meat stock and served with sour cream. This soup is usually made with beets, spinach or cabbage and may be served hot or chilled.

Bulke (Bulkie)—Large, light yeast roll.

Challah (Cholla)—Loaf of very light white bread, most commonly braided, prepared especially for the Sabbath or holidays.

Bubke—Coffee cake.
Cholent—A combination dish of fat beef, potatoes and dried beans, baked slowly in the oven to be served on the Sabbath.
Farfel—Noodle dough grated into barley sized grains and served in soup. During Passover, crumbled Matzoh is used as farfel.
Fleischig—Term describing meat or meat products.
Gefillte Fish—Highly seasoned chopped fish mixture, usually stuffed into the fish skin.
Hamantaschen—Three cornered cakes with pastry or cookie crust and filled with poppy seeds, dried fruit or cheese; traditional for Purim.
Helzel—Skin of poultry neck filled with rich bread or oatmeal stuffing.
Kasha—Buckwheat groats served as a cooked cereal or as a potato substitute with meat gravy.
Kichlach—Light egg cookies.
Kishke (or derma)—Beef casings stuffed with a rich seasoned filling and roasted.
Kosher (Kasher)—Fit or proper to eat according to the ritual of the Jewish dietary laws.
Knaidlach or Kloese—Dumplings, usually served in chicken soup. During Passover these are made with Matzoh meal and are traditional for the Seder.
Knishes—Pastry filled with ground meat.
Kreplach—Noodle dough filled with ground meat or cheese filling, similar to Italian ravioli.
Kuchen—Coffee cake..
Kugel—Pudding, common types are made with potatoes or noodles.
Latkes—Pancakes; potato latkes are especially popular.
Leckach—Honey cake traditional for Rosh Hashanah.
Lox—Smoked and salted salmon.
Lukshen—Noodles, usually used in "lukshen kugel" (see kugel) or in chicken soup.
Matzoh—Flat unleavened cracker used in place of bread during Passover.
Matzoh Meal—Finely ground matzoh used in cooking and baking primarily during Passover. Matzoh meal is often used in cooking especially in preparing meat loaf, all through the year.
Milchig—Refers to milk and milk products.
Mohn—Poppy seed.
Nahit—Chick peas served as salted nuts.
Pareve—Refers to neutral foods like fish, eggs, fruit and vegetables which are permissible to use with meat or milk meals.
Pirogen (*Piroshkes*)—Yeast dough or pastry filled with stuffing
Rusell—Naturally fermented beet juice used as vinegar during Passover, especially in making borsht.
Schav—A soup similar to borsht made from sorrel grass.
Schmaltz—Rendered fat, usually chicken fat, commonly used in cooking.
Strudel—Thin pastry rolled up with fruit and nut filling.
Teiglach—Small balls of sweet dough cooked in honey.
Tzimmes—Pudding usually made with prunes, carrots or sweet potatoes and fat meat.

ACKNOWLEDGMENTS

The author wishes to thank Miss Sybil Kaplan, nutritionist at Beth Israel Hospital, Boston, and Rabbi David H. Wice of Congregation Rodeph Shalom, Philadelphia, for their helpful suggestions and comments.

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Nutrition Briefs

A METHOD for the control of lipemia in familial hyperlipemia is presented. The patient rigidly restricts the ingestion of fat for a period of approximately 30 days and then is allowed one fatty meal during each twenty-four hours. Blood lipid analyses distinguish familial hyperlipemia from essential familial hypercholesterolemia—a condition in which dietary fat restriction has no effect.

—C. F. Wilkinson, Jr. *Ann. Int. Med.* 45: 674, 1956.

ACIDOSIS increases and alkalosis decreases the serum potassium concentration independently of changes in intracellular potassium. For every 0.1 unit change in extracellular pH there was an average inverse change of 0.6 meq per L in the serum potassium concentration.

—J. M. Burnell, M. F. Villamil, B. T. Uyeno and B. H. Scribner. *J. Clin. Investigation* 35: 935, 1956.

OROTIC acid protected rats against the deleterious effects on animals and offspring of a diet devoid of "animal protein factor." Administered without orotic acid prophylaxis, the diet led to a 72 per cent mortality in the first generation, 100 per cent in the second. With orotic acid supplementing the deficient diet, mortality was reduced to 7 per cent in both generations.

G. Moruzzi, M. Marchetti, R. Viviani, and A. Rabbi. *Intern. Ztschr. f. Vitaminforsch.* 26: 328, 1956.

GLUCAGON markedly depressed basal pancreatic secretion as well as secretion stimulated by secretin in acute experiments on dogs.

—L. Walker and H. Necheles, *Am. J. Physiol.* 187: 638, 1956.

THE EFFECT of 1 g of bioflavonoid and/or 200 mg of ascorbic acid, administered daily, in aborting or curing the common cold was tested in a controlled double-blind trial on over 1,900 subjects. No appreciable effects were observed after three days on subjective or objective improvement.

—H. E. Tebrock, J. J. Arminio, and J. H. Johnston. *J. A. M. A.* 162: 1227, 1956.

THE administration of a bioflavonoid had effect neither on the incidence or cure of colds nor on the ascorbic acid level of the blood in a controlled study on 89 medical students and nurses.

—W. L. Franz, G. W. Sands and H. L. Heyl. *J. A. M. A.* 162: 1224, 1956.

FERTILITY is distinctly lowered by vitamin deficiencies. When pregnancies occur in deficient animals the disturbed fetal development can be seen by the reduced rate of weight gain of the pregnant animal. Those young carried to term in spite of maternal deficiencies are below normal birth weight, frequently show serious injuries, have a high postnatal mortality, and can rarely be weaned.

—H. Pfaltz and E. L. Severinghaus. *Am. J. Obst. & Gynec.* 72: 265, 1956.

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—G. W. Atkinson and W. C. Kappes, Jr. *Virginia M. Month.* 83: 391, 1956.

PROTEINS with a superior growth-promoting value, formed greater amounts of liver protein than those of inferior growth-promoting value. The superior growth promoters formed lesser amounts of glycogen and fats and vice versa.

—R. G. Chitre and S. M. Vallury. *Indian J. M. Res.* 44: 565, 1956.

CHLORPROMAZINE inhibits basal gastric secretion and the adrenal phase of secretion induced by insulin hypoglycemia. Elorine sulfate® with chlorpromazine had a synergistic inhibitory effect.

—D. C. H. Sun and H. Shay. *Am. J. Physiol.* 187: 635, 1956.

AFTER three weeks of corn oil (one ounce three times daily and as cooking and salad oil) serum cholesterol levels were significantly lower in all of a group of 23 patients with coronary artery disease.—L. Tobian and N. Tuna. *Clin. Res. Proc.* 5: 182, 1957.

Reviews of Recent Books

The Premature Baby, by V. Mary Crosse, Little, Brown, Boston, 1957, pp. 242, $5.00.

Any book about prematures and prematurity, even a new edition of an old book, must be sufficiently different from the standard texts on the subject by Dunham, C. A. Smith or The American Academy of Pediatrics, to warrant publication. The fourth edition of Dr. Crosse's book is a very worth-while addition to the literature on the care of prematures.

The chapters, "Management and Care," "Hospital Care," "Home Care," "Clothing" and "Feeding," will be found equally valuable to nurses and doctors caring for these immature infants. The author gives statistical proof of the impracticality of handling a premature nursery in a hospital where there are fewer than 600 deliveries each year. The author's experience with the electrophrenic respirator in infants with pulmonary disease may encourage more people in this country to try its use for respiratory problems in the premature. Valuable "rule-of-thumb" formulae are given for such things as weight gain, feeding, fluid and drug calculation, obviously derived from her own extensive experience. While the feeding instructions with proprietary foods are of British manufacture, the principles are easily translated to similar American products.

The author's experience with the feeding of human milk to premature infants is one of the most impressive and best documented available today. Her evidence indicates the superiority of human milk in lowering both morbidity and mortality in the nursery and also in lowering morbidity when the child leaves the nursery. Previous objections that human milk contains too little calcium for the premature are disproved.

Certain controversial topics are dispensed with too dogmatically. For example, the rocking bed is dismissed with a word, face masks are listed as essential, frequent small feedings are recommended, and most physicians caring for prematures in this country would find that the author's recommendation for fluid therapy contains too much salt. A few inconsistencies are found in this volume. For example, in one section the author recommends early clamping of the cord in order to prevent pulmonary edema and later she recommends late clamping of the cord in order to prevent anemia. Likewise, in one section prothrombin deficiency is suggested as the cause of hemorrhagic disease of the newborn and later the presently acceptable factor VII is listed as the main cause of hemorrhagic disease. The author's use of transfusions when the hemoglobin is less than 7 g per 100 ml would be questioned in this country.

One wishes that the author had expressed her opinion of a few other controversial subjects, such as the use of ultraviolet lights in the prevention of infection in the nursery, or the use of prophylactic chemotherapy in infants born of infected mothers. A somewhat more detailed analysis of the physiology of the premature would make this book more helpful to students.

The chapter, "Complications Liable to Occur in the Premature Baby," contains a most thorough analysis of almost all of the problems in the care of prematures and is an up-to-date compendium of our handling of these problems today. This section alone should make this book extremely valuable.

This small book is very well written, lends to easy readability, and is a valuable addition to the pediatric literature. It should be available to all those desiring a better understanding of prematures.

L. A. BARNESS

Biochemistry of the Amino Acids, by Alton Meister, Academic Press, New York, 1957, pp. 485, $10.00.

Here is a book that should prove most welcome to biochemists, nutritionists, clinical investigators, and to all students in biochemistry and nutrition. It is written in an easily readable style. For instance, much of the information in the book is presented in historical sequence, which whets the reader's interest. Pertinent quotations from outstanding investigators add spice. The subject matter, which is well chosen, includes discussion of the role of the amino acids in nutrition, intermediary metabolism of the amino acids in normal and pathologic conditions as well as other general biochemical and physiologic considerations. The scope of the book is indicated by 2,859 references to the original literature; this greatly adds to its usefulness.

O. M. HELMER

Cholesterin-Ernährung-Gesundheit (Cholesterol, Nutrition, Health), by Wilhelm Halden and Ludwig Prokop, Urban & Schwarzenberg, Vienna, 1957, pp. 88, DM 9.

Cholesterol metabolism, diet, and their relationship to the etiology of coronary heart disease engage so many investigators and provoke so much controversy in the United States that this area of research may seem to be almost a domestic preserve. This little monograph by Professor Halden and Doctor Prokop is evidence, however, that others besides Americans are also intensely interested and, moreover, are well informed about the present state of knowledge. Halden and

Prokop have actually managed to provide a more complete and better balanced review than anything currently available in English. Though most of their discussion is based on American research, they cite enough European literature to remind us that our colleagues abroad have contributed much in the past and are again becoming active in this field.

In only 73 pages of text it is impossible, of course, to provide a critical discussion of the whole subject, or even of the major developments of the past decade; nor is the time yet ripe for final conclusions about some of the problems of greatest concern. But the authors have managed to pack into a small space a great deal of information that will be useful to the general medical public as well as to the research workers. The organization of the material into many short sections and a liberal provision of tables and graphs make for easy intelligibility for anyone with only a modest knowledge of German. There is a minimum of detailed argument about pros and cons and a maximum of simple presentation of facts. The whole treatment is conservative yet permeated with the authors' realization that in this field and its burgeoning development there may be profound significance for the future public health. A. K.

Alcoholism, edited by George N. Thompson, Charles C Thomas, Springfield, Ill., 1957, pp. 536, $9.50.

For those interested, not only in the problem of the alcoholic as an individual, but also in the situations he creates for society and the physician, the Thompson monograph should find a valued place.

The eight chapters are written by 11 outstanding individuals long recognized for their research efforts and the reporting thereof. The book of more than five hundred pages presents a mass of material in condensed form which, if expanded, might possibly have taken two or three volumes of similar size. Chapter titles in a book review make for uninteresting reading as a rule, but presenting the gist of each section title in this review, I believe, will give a bird's eye view of the important phases covered.

The social and public health aspects are covered by Hirsh in a 100-page treatise. Among the subjects discussed are nosology; statistics; alcohol and women, marriage, divorce, delinquency, promiscuity, venereal disease, crime, and traffic accidents; and "A. A." Harger, the "inventor" of the Drunkometer, discusses the pharmacology of alcohol in "good-reading" yet comprehensive fashion. This is followed by a well-done discussion of the pathology of alcoholism of Edmonson and his associates. The chapter by Himwich ably embraces alcohol and cerebral physiology while Olsen presents current views on the role of alcoholism in internal medicine, stressing a variety of clinical conditions caused or aggravated by alcohol. He admonishes that alcohol should be regarded as a habit-forming drug; a narcotic, rather than a stimulant. Nielsen presents the neurologic aspects of alcoholism, and Thompson, the editor of the book, discusses the psychiatry of alcoholism. The neurologic, psychiatric, and medical aspects of the clinical discussion perhaps could have been considerably enlarged upon to the benefit of the clinician. Because of the influence of alcohol upon the brain a worth-while contribution is the chapter by Marinacci on electroencephalography in alcoholism. Sample E.E.G.'s are presented from representative case reports. That chronic alcoholism and hepatic cirrhosis are definitely associated is regarded as reasonably conclusive. Therapy in neurologic and psychiatric problems is briefly discussed, and the drugs used in treatment of alcoholism and their presumed pharmacologic action are reviewed.

The importance of and the frequency of the occurrence of malnutrition in chronic alcoholism might have been stressed and enlarged upon to a greater extent. This well-documented survey can, however, answer the needs of many, other than physicians, for factual information on this serious problem as it influences the patient and his community. C. G. WEIGAND

Alcoholism. Basic Aspects and Treatment, edited by H. E. Himwich, Am. Assn. Advancement of Science, Washington, D. C., 1957, pp. 220, $5.75.

The subject of alcoholism is so important in modern life that any intelligent appraisal by qualified experts deserves careful consideration. This applies to this publication which presents a symposium held under the auspices of the American Association for the Advancement of Science in co-operation with the American Psychiatric Association and the American Physiological Society, at the meeting in Atlanta, Georgia, December, 1955.

The complexity of the problem is presented from different viewpoints in 19 papers. There is a study of the depressing effects of alcohol on the oxygen consumption of brain slices; a discussion of the pathway of alcohol metabolism; chapters on vitamin deficiencies and the effects of vitamin intake on carbohydrate metabolism under conditions of alcohol administration. Among the papers dealing with the therapeutic aspects are those dealing with new drugs that have recently been recommended. It is interesting that several authors reported essentially similar successful experiences with different tranquilizing agents. The editor's (Himwich) summary is particularly valuable. Although the problems of alcohol remain largely unsolved, it is encouraging to see such valiant attempts at its solution.

S. O. W.

Soybeans for Health, Longevity, and Economy, by Philip S. Chen, The Chemical Elements, South Lancaster, Mass., 1956, pp. 241, $3.00.

Soybeans have been recognized by nutritionists as a valuable contribution to the food economy, and their increased use in the American diet has been encouraged sporadically. This book represents a highly enthusiastic appeal for including soybeans in the dietary. Many recipes utilizing soy products should be of interest to

the homemaker. Information concerning the cultivation and preservation of soybeans, and some of the technics for processing soybeans for the various food products is conveniently placed for reference.

The nutritive contributions which soybeans make are discussed in considerable detail. The work of many investigators is cited, but unfortunately the author has not always listed the references. The reader who would wish to have further detail about specific studies would experience some difficulty in locating the sources.

Broad conclusions are frequently drawn from the data of experiments conducted under highly specific circumstances. The lay person especially is unable to make judgments concerning these statements, and thus food faddism is encouraged. For example, liberal use of soybeans is said to "insure the individual user health, longevity, and economy" (p. iv), a claim which is obviously too broad. To compare percentage concentrations of calcium in liquid milk and in soybeans (p. 26) without relating them to the amounts of the respective foods which might be consumed daily is misleading. The statements that choline prevents "certain types of kidney damage and arteriosclerosis" (p. 35) and that pantothenic acid has "reported ability to cure certain types of gray hair" (p. 35) fail to make clear to the reader that these deficiency symptoms are the results of severe dietary lacks in certain animal species. Illustrations pertaining to the cost of nutrients, such as the one for fat equivalents (Fig. 5, p. 17), are misleading in that the foods used for comparison are not, in many instances, those upon which the diet depends for the nutrient in question; for example, bread, dried peas, and corn meal are not significant sources of fat nor should their values in the diet be judged on the fat content.

A chapter on soybeans and disease is seriously misleading. The opening paragraph of this chapter includes these statements:. . ."it (soybean) also prevents or cures many of the common diseases. . . . Among these common diseases may be mentioned coronary disease, arteriosclerosis, diabetes, intestinal disturbances, and diseases due to food allergy" (p. 54). Many readers may be encouraged by the statements included in this chapter to substitute injudicious tampering with their dietaries for the professional advice which their state of health may require. Others, whose primary motive is profit, will use these statements to justify the sale of soy products at exorbitant costs.

The author is, undoubtedly, sincerely interested in a more important place for soybeans in the world dietary at low cost. However, it is to be regretted that many physicians and nutritionists will find it necessary to carefully interpret the contents of this book to their patients.

C. H. ROBINSON

The Physiology and Biochemistry of Lactation, by S. J. Folley, Oliver and Boyd, Edinburgh, London, 1956, pp. 153, $3.75.

A series of lectures given by the author at the Collége de France in 1953, and published the following year as "*Recherhes Recéntes sur la Physiologie et la Biochimie de la Sécrétion Lactée*" has now been translated and brought up to date. The English title is misleadingly comprehensive, since the contents are limited very largely to the results of recent research at the National Institute for Research in Dairying at Reading, England. Those aspects of lactation discussed are: the hormonal basis of mammary gland development in a range of species from mice to cows, the initiation of milk secretion and its hormonal maintenance, including recent information on adrenal and thyroid effects, the physiology of milk ejection and the biosynthesis of milk fat, lactose, and protein. Too concentrated for easy fireside reading, this review is nevertheless clearly presented and there is a valuable bibliography. The many illustrations are excellent.

Although primarily intended for physiologists and biochemists in the veterinary field, the author in his preface, expresses the hope that the book will also be useful to medical students. In fact, it will be of little practical value for the doctor and it is perhaps a pity that the opportunity was not taken to enlarge its scope to include what is known of human lactation.

F. E. HYTTEN

Health Yearbook, 1956, edited by Oliver E. Byrd, Stanford University Press, Stanford, Calif., 1957, pp. 278, $5.00.

The editor of this annual Health Yearbook, now in its 14th edition, undertakes each year the stupendous task of screening the vast literature in the fields of public health, medicine, and the allied sciences. Dr. Byrd, in the preface to this edition, states that he read "slightly fewer than 2,000 articles in well over 300 different health journals. . . .". From this he made "a final selection of 254 articles" which he considers to be "a representative sample of the published health literature for the year 1956."

The editor has condensed into readable and good reference form much that unquestionably is useful for public health workers for whom the work is apparently intended. This includes a breakdown of vital statistics, socio-economic factors in health and disease, advances in the mental health area, progress in the diagnosis and conquering of infectious disease, chronic and degenerative disorders; narcotics, alcoholism, etc. Résumés of available health services are presented and the concluding chapters are devoted to health within the family, school, industry, community, and on the international scene.

Throughout the years of its publication the book unquestionably has proved of merit in providing keys to current developments in the fields it represents. The ultimate value of such a book is based upon the reader's use of these keys.

C. I. P.

Practical Nutrition, by Alice B. Peyton, J. B. Lippincott Company, Philadelphia, 1957, pp. 409, $3.60.

The stated purpose of this book is to "fill a need for a simple and practical presentation of nutrition, diet therapy, and food economics." The book has been written primarily for students in practical nursing, and secondarily for homemakers and other lay persons who wish authoritative information. The author has had considerable experience in teaching at the secondary and college level and is especially qualified for teaching nutrition to nursing students.

The goals to be realized in the nutrition education of practical nurses have not been, for the most part, clearly defined. Therefore, to write an appropriate text in dietetics for these students is a challenge not easily met. This book appears to be largely a condensation of material already presented in a number of texts used for professional nursing students. This approach is not wholly successful inasmuch as the selection has not always been limited to that which the practical nurse might be expected to use. As a consequence, matters important for the student are too briefly presented. For example, the practical nurse might be expected to prepare the patient's meals in the home situation; even though a cookbook is available, she would need some guidance in cooking for one (or two) and in making the adaptations for certain therapeutic diets. This book might have amplified such important material perhaps at the expense of some of the discussion of symptoms, etc.

The author is to be commended for the emphasis placed on the dangers of food faddism, and for the helpful section on budgeting. The information in the book appears to be correct, but there are a number of ambiguous statements and inconsistencies which detract from the book as a whole. For example, the Basic Seven food grouping is emphasized throughout, but the table quoted on pages 71–74 does not follow this grouping and is likely to confuse the reader. The rearrangement of the Food Exchange Lists is unfortunate; for example, in the meat list, the reader is informed (page 197) that 3 oz is an average serving of meat, but the author proceeds to give equivalents for 2 oz. Statements relating to rickets (page 58) are misleading in that calcium deficiency has not been an important etiologic factor in this country. The sodium restricted diet does not take into consideration the newer tables of sodium values published by the National Research Council in 1954.

Study questions at the end of the book might have been more conveniently placed at the end of each chapter. The 11-page list of supplementary references is unnecessary since it is, for the most part, a listing of chapter numbers of books already listed on pages 364–367. With a selection of reference books available, any instructor or student can select the supplementary readings as needed.

In spite of these few criticisms, it is recognized by this reviewer that this book represents worth-while step in the direction of the more satisfactory nutrition education of the practical nursing student.

C. ROBINSON

Books received for review by THE AMERICAN JOURNAL OF CLINICAL NUTRITION are acknowledged in this column. As far as practicable, those of special interest are selected, as space permits, for a more extensive review.

The Functions and Education of Medical Record Personnel by the Study Group of the Graduate School of Public Health of the University of Pittsburgh, Univ. of Pittsburgh Press, Pittsburgh, 1957, pp. 78, $2.00.

Technique of Fluid Balance by Geoffrey H. Tovey, Charles C Thomas, Springfield, Ill., 1957, pp. 100, $2.50.

Medical Writing (third edition) by Morris Fishbein, McGraw-Hill, New York, 1957, pp. 262, $7.00.

Calcium Metabolism by J. T. Irving, John Wiley and Sons, New York, 1957, pp. 177, $2.75.

Biochemistry (second edition) by Abraham Cantarow and Bernard Schepartz, W. B. Saunders, Philadelphia 1957, pp. 867, $12.00.

Abstracts of Current Literature

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POTASSIUM METABOLISM

The protective action of glutathione against the lethal effects of a rapid rise of serum potassium concentration is an observation which may have clinical importance. (See also this JOURNAL 5: 589, 1957)

Combined Action of Potassium and Histamine on Mice and Guinea Pigs. R. L. Zwemer, J. J. Martorano, and R. Truscoe. *Am. J. Physiol.* 184: 479, 1956.

When body cells are damaged by force, burns, lack of oxygen, or decreased blood supply, they release substances which in large enough quantities induce shock often resulting in death. Two of these substances have been identified as histamine and potassium. Either of these when injected into normal intact animals can induce shock and death. The lethal dose curves for each of the two agents when given in solution intraperitoneally to mice and to guinea pigs were determined. Potassium toxicity was quite comparable in both species, but histamine resistance in mice was more than 100 times that of guinea pigs. When both histamine and potassium are combined in a single injection the mortality rate goes up. The addition of a small amount of one will increase the toxicity of a known amount of the other to a point much greater than the sum of each given separately. A variety of combinations of both were tested in about 1,600 mice and about 500 guinea pigs. The results suggest that in future studies of traumatic and anaphylactic shock the simultaneous blood levels of both substances should be determined. Further experiments gave evidence that enhancement of toxicity diminished when the two agents were injected separately and that a plasma potassium rise did not follow histamine injection in all species. Glutathione which has been shown to protect against potassium, also had a protective action in mice against the histamine-potassium combination. An antihistaminic (Chlor-Trimeton®) which protected guinea pigs against histamine alone did not protect them or mice against the combination. AUTHORS

Sodium, Potassium and Nitrogen Balances in Chronic Nephrectomized Dogs. C. R. Houck. *Am. J. Physiol.* 185: 175, 1956.

Twelve bilaterally nephrectomized dogs on a low-salt, 54 cal/kg/day diet were maintained for periods up to three weeks by intermittent peritoneal dialysis. This procedure maintained the animals in normal sodium balance but provided both a negative potassium and nitrogen balance. The overall loss of potassium occurred even though the dialysate potassium concentration was varied from 2.8 to 3.7 meq/liter. It is believed that the negative K and N balances are brought about by loss of plasma protein and some erythrocytes into the peritoneal dialysate. The data indicate that K and N are not lost from the body in the same ratio that they occur in tissues. Renoprival hypertension develops despite failure of the body to retain sodium and despite loss of both potassium and nitrogen from the body. AUTHOR

FATS AND COAGULABILITY OF BLOOD

The influence of dietary fats upon the clotting of blood has been studied by several groups of investigators in this country with sharply divergent results. The results obtained by Duncan and co-workers indicating a lowering of clotting time after a fat meal were disputed by Wright et al. who were unable to demonstrate increased coagulability. The latter position has been supported by other investigators. However, Keys has shown recently that blood clotting is enhanced by fats. The following abstracts from the British literature support this view in part. In addition,

some evidence is supplied to indicate the actual constituents which may directly influence the clotting mechanism.

Food Lipids and Blood Coagulation. N. F. Maclagan, and J. D. Billimoria. *Lancet* 2:235, 1956.

The effect of adding a variety of fats to plasma *in vitro* was studied in relation to the accelerated clotting time ("Stypven" time). The most active fats were milk products, particularly butter, cream and cheese. Most margarines had a relatively slight effect and other animal fats, vegetable fats and eggs had no effect.

The difference between butter and margarine was confirmed in a series of seven subjects, where both accelerated and whole blood clotting tests indicated that butter considerably lowered the clotting time, whereas a margarine meal did not. It is suggested on the basis of preliminary tests that various phospholipids in the milk are the active agents. F. E. HYTTEN

Effect of a Meal of Eggs and Different Fats an Blood Coagulability. J. R. O'Brien. *Lancet* 2:232, 1956.

The clotting time of plasma, when accelerated by Russel's viper venom ("Stypven" time), varies proportionately with the amount of thrombin generated in platelet-poor plasma and with the clotting time of whole blood in silicone-lined tubes.

Eight male subjects, 49 to 83 years of age, convalescing from tuberculosis and four who were bedridden with chronic medical diseases, were given experimental diets of tea and toast plus 50 g of butter or margarine or cooking fat and two boiled eggs. Ingestion of the 50 g of fat shortened the Stypven time by about one-quarter, due probably to an increase of phospholipoids such as phosphatidyl ethanolamine. Ingestion of the eggs, containing about 10 g of fat and 3 g of phospholipoid produces a similar shortening of the Stypven time. "The phospholipoid content of a fatty meal may be as important as the quantity or character of the fatty acids it contains." F. E. HYTTEN

Reassessment of Effect of Fatty Meals on Blood Coagulability. G. H. Hall. *Brit. M. J.* 2:207, 1956.

It has been suggested that blood coagulability is increased after a fatty meal and that thrombi may form in such circumstances. This paper notes that the supposition rests on the results of experiments in which coagulation is studied in silicone-lined tubes, where the effect of platelets is minimized. Experiments performed with plain glass tubes and with platelet-rich plasma show no difference in clotting time before and after a fatty meal.

Since intravascular thrombosis favors certain areas, it is likely that vessel-wall damage is primary and that platelets are therefore an important factor in the clotting; the theory of the relationship of intravascular thrombosis to alimentary lipemia is criticized in the light of these results. F. E. HYTTEN

Phospholipids from Brain Tissue as Accelerators and Inhibitors of Blood Coagulation. P. Barkhan and M. J. Newlands. *Lancet* 2:234, 1956.

A briefly described chemical fractionation of human brain tissue produced two phospholipid materials active in coagulation systems. One was an accelerator, probably phosphatidyl ethanolamine; and the other an inhibitor, probably phosphatidyl serine.

F. E. HYTTEN

The inhibition of fibrinolysis by fat feeding is an interesting observation which may indicate that the activity of proteolytic enzymes, such as plasmin, can be influenced by serum lipid concentrations.

Inhibition of Fibrinolysis by Alimentary Lipaemia. H. B. W. Greig. *Lancet* 2:16, 1956.

The author believes that the body normally deals with intravascular thrombi by fibrinolysis and that incorporation of the clot into the vessel wall implies failure on the part of the body to lyse the clot.

Fibrinolysis *in vitro* was tested after a fat-poor and a fat-containing meal in the plasma of 12 men and 13 women, aged from 19 to 56 years, and all healthy. The presence of fat in the plasma considerably retarded fibrinolysis *in vitro*. The addition of cream to plasma had a similar effect, and this could be reversed by "clearing" the plasma with heparin. The effect of physical exercise after a heavy fat meal was to reverse the fat inhibition of fibrinolysis.

As an addendum to the paper it is said that further work indicated that the ingestion of unsaturated fats does not inhibit fibrinolysis. F. E. HYTTEN

NUTRITIONAL VALUE OF LYSINE SUPPLEMENTATION

Divergent opinions have been expressed concerning the value of lysine supplementation as a growth stimulant and as a factor in improving nitrogen utilization in the diets of children or in diets consisting largely of vegetables. While evidence has been presented supporting the positive effects of lysine supplementation, the work of McCance has shown that the simple addition of bread to a deficient diet may provide an excellent growth response in undernourished children. The use of lysine additions to the diets of children must be very carefully evaluated over a long period before recommendations favoring it can be made. Lysine-supplemented products are already commercially available.

Lysine and Methionine Supplementation of All-Vegetable Diets for Human Adults. D. M. Hegsted, M. F. Trulson, H. S. White, P. L. White, E. Vinas, E. Alvistur, C. Diaz, J. Vasquez, A. Loo, A. Roca, C. C. Cohazo, and A. Ruiz. *J. Nutrition* 56:555, 1955.

Nitrogen intake and excretion data for young adult subjects consuming all-vegetable diets with and without supplements of lysine and methionine are presented.

The essential amino acids of the diet were determined. Young women, student dietitians of the Escuela de Dietistas of the Hospital Obrero, Lima, Peru, were the subjects.

An all-vegetable diet supplying 25 g of protein per day, of which 48 per cent of the protein came from wheat products and 62 per cent from cereals, contained all of the essential amino acids in quantities equaling or exceeding Rose's estimated minimum requirements. The amount of methionine plus cystine barely equaled the estimated requirement.

Supplementation of the diet with lysine improved the nitrogen retention following a depletion period, and methionine-plus-lysine supplements appeared to improve the retention still more. These data are interpreted as demonstrating improvements in biological value of the dietary protein. Considering the relative ease with which the subjects approached nitrogen equilibrium on the unsupplemented diet, the likelihood of protein or amino acid deficiencies in an adult population consuming diets essentially of vegetable origin does not appear to be very great.

The authors conclude from this study the probability that the proteins of fruits and vegetables which are usually not considered to be of importance in protein nutrition may be an important supplement to the cereal proteins.

It should be pointed out, however, that no such sweeping conclusions can be made on the relative values of vegetable and animal proteins from the short-time nitrogen retention experiments, but long-time experiments are also needed on growth, blood formation, on enzymic and hormone efficiency, and on resistance to infections. Such criticism can also be applied to all human amino acid studies in which only nitrogen balance experiments are carried out, particularly when conclusions are made on amino acid deficiencies in the American diet. B. SURE

The importance of the relative amino-acid composition of foods is illustrated in the concept of amino-acid imbalance. A variety of metabolic disturbances and growth failures have been produced in experimental animals by the feeding of single amino acids. An excess of one amino acid may (1) produce a relative deficiency of another, or (2) prove to have a toxic action, or may (3) increase the requirements of additional amino acids. In the following reports lysine supplementation is not recommended.

Lysine Requirements and Lysine Supplementation. S. E. Snyderman, L. E. Holt, Jr., P. M. Norton, and D. L. Fowler. *Proc. Am. Pediat.* Soc., Buck Hill Falls, Pa., May 9, 1956.

These investigators have utilized a synthetic diet in which the only variable involved was the amount of L-lysine. Six infants were studied and the daily requirement was found consistently to be 90 mg/kg. This amount is supplied by breast milk under ordinary circumstances with an adequate margin of safety. These findings are to be contrasted with a reported daily requirement of 170 mg/kg. It is pointed out that supplementation of diet with a single amino acid may be dangerous in terms of increasing requirements or losses of other important amino acids. They conclude that available evidence does not justify the supplementation of infant dietaries with lysine. T. C. PANOS

Commentary—Use of Amino Acids as Dietary Supplements. Amino Acid Imbalance and Lysine. *Pediatrics* 17:965, 1956.

The importance of fortification of foods with accessory factors (e.g., vitamin A, vitamin D, B-vitamins) as a control measure in prevention of deficiency disease is emphasized. In the case of protein supplementation, a specifically balanced intake of essential amino acids is known to be important and both deficits and excesses of particular amino acids may cause difficulty. The margin of safety in response to variation in amino acid intake is very much less than in the case with vitamins. Therefore, evidence of the need for and safety of single amino acid supplementation must be established before recommendations can be made. Neither of these desiderata has been convincingly demonstrated. Infants ingesting considerably less than the allegedly required 170 ± 30 mg/kg are known to thrive (e.g., breast-fed infants and those taking so-called "humanized" cow's milk preparations). Furthermore, recent work by Holt and co-workers indicates that the requirement for lysine is about 90 mg/kg. In addition, experimental evidence derived from studies on rats, humans, and human tissue culture indicate the dangers likely to accrue from ingestion of "even relatively small surfeits of lysine." The undesirability of promoting supplements of lysine in human nutrition becomes apparent and the "premature and irresponsible efforts to promote such reinforced products before adequate scientific data is available are particularly to be deplored." T. C. PANOS

The use of algae as cheap sources of protein for improvement of diets in those areas of the world deficient in protein foods is under study. The amino-acid content of algae is such that appropriate supplementation of the limited supply available in restricted vegetable diets would be provided.

Algae as Sources of Lysine and Threonine in Supplementing Wheat and Bread Diets. J. M. Rundley, R. B. Ing, and R. W. Krauss. *Science* 124:536, 1956.

Green algae (*Chlorella* and *Scenedesmus*) were mass-cultured, harvested, dried, ground to a powder, and fed to weanling rats. Under the conditions of the experiment described, algae as supplements to enriched wheat diets proved to be quite satisfactory as sources of amino acids. Chlorella is particularly rich in threonine. There may well be considerable potential application of algae protein as nutritional supplements. S. O. WAIFE

The lysine requirements for women appear to correspond fairly well to those of men as shown in the following report.

Nitrogen Balances of Women Maintained on Various Levels of Lysine. E. M. Jones, C. A. Baumann, and M. S. Reynolds. *J. Nutrition* 60: 549, 1956.

Rose and associates have reported that the minimal intakes of L-lysine which permitted nitrogen balance in six young adult men on a synthetic ration ranged from 0.4 to 0.8 g per day. The present paper presents nitrogen balance data of women maintained on a semisynthetic diet furnishing various levels of lysine.

The effects of various levels of lysine intake on nitrogen balance were studied in 14 women maintained on a semisynthetic diet in which about 95 per cent of the total nitrogen was furnished by pure amino acids and diammonium citrate. From data obtained in this experiment, it appears that 0.40 to 0.50 g lysine per day is adequate for the establishment of nitrogen balance in women under these conditions. B. SURE

MEGALOBLASTIC ANEMIA

The maturation of the erythropoietic cells depends upon the presence of vitamin B_{12} and folic acid. Deficiencies in either or both of these factors result in maturation arrest within the bone marrow and release into the circulating blood of abnormally large erythrocytes of shortened life span. The clinical states producing deficiencies in these factors are multiple and, for the most part, involve absorptive defects in the gastro-intestinal tract. Exceptions to this include the megaloblastic anemias of infancy, pregnancy, and scurvy, each of which is improved by use of folic acid. For a review of the classification of these anemias and current advances in diagnosis the following paper is recommended.

The Megaloblastic Anaemias. Their Investigation and Classification. R. H. Girdwood. *Quart. J. Med.* 25: 87, 1956.

The megaloblastic anemias are classified into a number of groups according to their primary antecedents, and new methods of diagnosis as, for example, serum vitamin B_{12} estimation, folic acid excretion, and vitamin B_{12} absorption, are shown to assist in investigation and classification.

This long paper constitutes a review of present knowledge, illustrated by cases from the author's wide experience. F. E. HYTTEN

Pernicious anemia following gastrectomy is observed only after a three year survival. The vitamin B_{12} requirement has been shown to be related to protein metabolism. The defective absorption of protein in gastrectomized patients may lower vitamin B_{12} requirements so that available stores are sufficient to maintain bone marrow activity for this period.

Incidence of Megaloblastic Anemia after Total Gastrectomy. L. D. MacLean and R. D. Sundberg. *New England J. Med.* 254: 885, 1956.

If pernicious anemia is due to an inadequate production of Castle's intrinsic factor which is produced in the stomach and is necessary for the absorption of vitamin B_{12}, this type of anemia should appear after total gastrectomy. In this paper 17 patients who had undergone total gastrectomy were studied. Megaloblastic anemia, indistinguishable from pernicious anemia, was found in all patients who lived for more than three years following the operation and received no prophylactic treatment. This anemia responded to parenteral vitamin B_{12} therapy. Since pernicious anemia occurs only infrequently after total gastrectomy, the authors suggest that this is due to a short duration of life after total gastrectomy and to prophylactic therapy usually given after such an operation. M. W. BATES

Weight Loss and Pernicious Anaemia. A. E. Read and R. Asher. *Lancet* 1: 882, 1956.

Cases are described to show that weight loss, caused by anorexia, may be commonly associated with Addisonian anemia. Severe weight loss with a clinical picture suggestive of malignancy may occur even before the anemia has become obvious, and it is suggested that pernicious anemia should be kept in mind in the differential diagnosis of otherwise unexplained loss of weight. F. E. HYTTEN

Megaloblastic Anaemia Following Partial Gastrectomy and Gastro-Enterostomy. J. Badenoch, J. R. Evans, W. C. D. Richards, and L. J. Witts. *Brit. J. Haematol.* 1: 339, 1955.

This paper describes the cases of six patients who developed megaloblastic anemia following operations for peptic ulcer, five after partial gastrectomy, and one after gastro-enterostomy. There were four men, 52 to 66 years of age, two women, 53 and 68 years of age. The anemia was diagnosed from 2 to 17 years after operation. The histologic appearance of the stomach is described for each case and excretion of acid and uropepsinogen, fat absorption, serum vitamin B_{12} and intrinsic factor secretion were estimated.

In five of the patients, there was atrophy of gastric body mucosa and the anemia was due to failure to absorb vitamin B_{12}. It was corrected by giving intrinsic factor. In the sixth case the pathogenesis of the anemia remained obscure. Steatorrhea was not a significant factor in any of the patients.

The pathogenesis of this condition, which occurs rarely after partial gastrectomy, is discussed. It is considered unlikely that the operation was merely incidental to a pernicious anemia, which would have occurred anyway, and it is suggested that chronic gastritis is the most likely common factor. F. E. HYTTEN

The following papers provide an interesting orientation in the current status of megaloblastic anemias in Great Britain. Early diagnosis of this condition in recent years has altered the clinical expressions of the disease and markedly improved the outlook for the patient.

Diet and Anemia. L. S. P. Davidson. *Proc. Brit. Nutrition Soc.* 15: 101, 1956.

The iron-deficiency anemias are probably a thousand times as common in Great Britain as are the megaloblastic anemias, and constitute, therefore, an infinitely more important social and economic problem even though they may not be so exciting from the academic point of view. The position is entirely different with the megaloblastic anemias in Great Britain. The number of persons suffering from megaloblastic anemia at the present time is considerably higher than it was 36 years ago. The reasons for this higher incidence are also obvious. First, the number of people between 60 and 80 years of age in Great Britain is much higher now than it was 36 years ago. Therefore, the number of people who are liable to develop Addisonian pernicious anemia is correspondingly greater. Second, the introduction of liver extract and later vitamin B_{12} has enabled patients suffering from Addisonian pernicious anemia to have a normal expectation of life. The total population of patients with pernicious anemia is therefore greater than ever before. Third, because of our increased knowledge of the pathogenesis of the megaloblastic anemias due to malabsorption, and our increased interest in, and recognition of, the megaloblastic anemias of pregnancy, many more of these patients are diagnosed and successfully treated today than 36 years ago.

At the present time pernicious anemia is diagnosed much earlier than formerly, hence the features of clinical jaundice, splenomegaly, acute glossitis and subacute combined degeneration of the cord, which were held to be of such diagnostic importance before liver therapy was introduced, are at the present time found in less than 5 per cent of the patients referred to the Blood Clinic in Edinburgh. We are still at a loss to know why one pregnant woman out of approximately 1,000, develops megaloblastic anemia. Often the cause does not seem to be due to direct dietary deficiency of folic acid. It does not follow that, because a patient has a macrocytic anemia, as judged by a high color index and a high mean cell volume he necessarily has a megaloblastic anemia. Also, it is apparent in Edinburgh that if a patient has a macrocytric anemia it is six chances to one he has a megaloblastic anemia. Third, if he has a megaloblastic anemia it is nearly six chances to one that he is suffering from Addisonian pernicious anemia. B. SURE

Clinical Picture of Pernicious Anaemia Prior to Introduction of Liver Therapy in 1926 and in Edinburgh Subsequent to 1944. Sir Stanley Davidson. *Brit. M. J.* 1: 241, 1957.

The author has had a particular interest in pernicious anemia prior to the discovery of liver treatment and in this paper he contrasts the clinical picture seen today with that prior to 1926. In a series of 250 cases since 1944 he finds that, compared to the earlier published series, many more older patients are being seen with a shorter duration of symptoms. He finds an opposite sex ratio to that described by Cabot in 1908 but this apparently has curious regional differences: females predominate by two or three to one in Scotland. This also occurs in Scandinavia and Germany, but in England and the United States males are apparently more often affected by the disease.

The classic textbook symptoms of jaundice, splenomegaly, acute glossitis, diarrhea and subacute combined degeneration of the cord occur rarely now and should no longer be given emphasis in textbooks. Dependence on such symptoms delays diagnosis which can be rapidly and accurately established by modern methods of blood examination. F. E. HYTTEN

Mucosal atrophy of the tongue, oral cavity and linings of the stomach have been described in pernicious anemia. This abnormality has been attributed to the lack of vitamin B_{12} necessary for normal cellular metabolism.

La Gastrite Atrophique du Fundus dans l'Anemie Pernicieuse Etude Biopsique. C. Debrary, R. Laumonier, F. Besaucon and P. Housset. *Archiv. d. Mal. de l'App. Digestif. et Mal. de l'Nutrition.* 44: 28, 1955.

The authors have studied the findings obtained by biopsy of the fundus of 50 patients affected with atrophic gastritis of pernicious anemia origin. These findings were compared with the biopsy of other atrophic gastritis not originating with pernicious anemia. This study has demonstrated that the lesions caused by pernicious anemia are the same as those found in ordinary atrophic gastritis. However, when associated with pernicious anemia the lesions are more extensive and severe; they are irreversible and chronic. The biopsy findings confirm the gastroscopic findings and the clinical and biologic observations.

J. JACOBSON

Rise of Serum Folic Acid Levels After Injection of Vitamin B_{12} in Nutritional Macrocytic Anaemia. M. S. Narayanan, K. G. Stenoy, and G. B. Ramasarma. *Nature* 178: 1347, 1956.

Folic acid and vitamin B_{12} have some biochemical similarities but there is little information about the effects of one on the other in the body. The effect of injections of folic acid on the serum vitamin B_{12} was noted in 13 patients with nutritional macrocytic anemia. Injected vitamin B_{12} for these patients, whose initial serum level was low, resulted in only a temporary rise, but administration of folic acid caused a prolonged rise in serum vitamin B_{12} within 24 to 48 hours. It is suggested that folic acid mobilizes body stores of vitamin B_{12}. F. E. HYTTEN

Among the usual criteria required for a clinical diagnosis of pernicious anemia is achlorhydria. However, in

the following report, free hydrochloric acid but no intrinsic factor could be demonstrated in gastric secretions. The administration of intrinsic factor alone would be of interest in this patient.

Pernicious Anemia in Childhood. T. D. Stevenson, J. A. Little and L. Langley. *New England J. Med.* 255: 1219, 1956.

Pernicious anemia is predominately a disease of adult life though a few cases have been reported in children. This paper reports the results of a study of a seven and one-half year old Negro boy with recurrent macrocytic anemia, megaloblastic bone marrow, free hydrochloric acid in the gastric juice and vitamin B_{12} deficiency.

The anemia was due not to dietary lack of vitamin B_{12}, competitive utilization of vitamin B_{12} by intestinal micro-organisms, or alteration in absorptive property of the intestine, but to the inability of the patient to absorb vitamin B_{12}, due to a lack of intrinsic factor. When gastric juice from the patient was administered with radioactive vitamin B_{12} to another pernicious anemia patient there was no absorption of the vitamin B_{12}. This showed that there was no intrinsic factor in the gastric juice.

An interesting finding of this study was the lack of achlorhydria in this pernicious anemia patient. There were similar findings in five of the six proved cases of pernicious anemia in childhood reported in earlier papers. This would indicate that the gastric lesions of pernicious anemia are due to vitamin B_{12} deficiency. If this is true, absorption studies with radioactive vitamin B_{12} should show a lack of intrinsic factor in a pernicious anemia patient before lesions of the gastric mucosa and achlorhydria develop. M. W. BATES

The possibility of a metabolic abnormality involving folic acid coenzyme induced by the excessive ingestion of barbiturate is presented. This is an important observation with wide implications since little information is available concerning the effects of commonly used drugs upon the many aspects of cellular metabolism.

Megaloblastic Anemia Due to Barbiturates. Q. J. G. Hobson, J. G. Selwyn, and D. L. Mollin. *Lancet* 2: 1079, 1956.

A case is described of a 30-year old psychotic woman who, after episodes of hospital treatment became addicted to the barbiturate "Tuinal" containing equal parts of amylobarbital sodium and quinalbarbital sodium. At the height of her addiction she was probably taking 18 to 20 grains daily. She was finally admitted to the hospital with a very severe megaloblastic anemia. Serum vitamin B_{12} was 265 μg per ml and absorption of labeled vitamin B_{12} was normal. Numerous other tests indicated no abnormality. There was no response to vitamin B_{12} but an immediate and lasting response occurred when 20 mg. daily of folic acid was given.

The evidence suggests that these barbiturates, like other related drugs, may interfere with the metabolism of folic acid. Such an anemia due to barbiturates must be very rare in view of their widespread use, but the possibility must be kept in mind. F. E. HYTTEN

The Effect of Development, Anaemia and Undernutrition on the Composition of the Erythrocytes. R. A. McCance and E. M. Widdowson. *Clin. Sc.* 15: 409, 1956.

The concentration in the red cell of water, hemoglobin, N, Fe, P, K and Na and Cl was studied in five normal adults, five newborn infants, three normal fetuses of about 18 to 20 weeks gestation, and seven severely anemic patients, with hemoglobin concentrations from 2.15 and 5.8 g/100 ml. A parallel study was made in nine healthy adult pigs, five newborn pigs, seven litters of pig fetuses and two severely undernourished pigs, held at a weight of 10 kg for eight months.

The following changes occurred in the red cell with increasing maturity: the concentration of water, Na, and Cl fell in both species, the concentration of N, hemoglobin, Fe and K rose in both species and the concentration of P fell in man and rose in the pig. There was no increase in the ratio of N/K with maturation.

Anemia in man raised the concentration of water, K and P, and lowered the concentration of N, hemoglobin and Fe. Na was unaffected. Prolonged undernutrition in pigs caused a lower concentration of hemoglobin, N, Fe and a higher concentration of water and possibly K. F. E. HYTTEN

FOOD TECHNOLOGY

Nutritionists are vitally concerned with the processing, storing, shipping, and preparation of foods since the nutritive value and acceptability of foods may be affected by any one of the phases required for these materials to reach the consumer. While it is true that the nutritive values may decrease somewhat in food processing, palatability is often enhanced and general availability of a wide variety of foods is achieved.

The Impact of Food Technology on the Nutrition of Man and Animals. G. F. Marrian. *Proc. Brit. Nutrition Soc.* 15: 142, 1956.

Food processing includes all treatments received by a foodstuff from its point of origin to the point in space and time at which it is consumed. Most foods are not fully edible, i.e., palatable as well as nutritious, in the form in which they are produced and require at least a heat treatment to transform them from potentially edible to edible. Food supplies are normally available, particularly for the industrialized minority of the world's population, from sources distant from the consuming populations. They must, therefore, be moved and stored in some form which permits them to arrive on the table in a condition both palatable and nutritionally sound.

Processing to render potential foods edible and to

preserve foods obtained in times of plenty for use in times of shortage has been practiced since before the beginning of recorded history. The difference between early methods of heat treatment, withdrawal of water, pickling and curing, and modern methods is that we now have more control over the treatments, more knowledge of their chemical and physical effects, and more certainty of producing foods of consistent palatability and known nutrient content.

A brief review such as this of the effects of processing on the nutrients in foods must leave an impression of losses of nutrients whenever a food is given any form of treatment. On the whole this is true, but it must be emphasized that the processing of foods is to a large extent a necessity to make them edible and palatable. It is also necessary for their transport from their sources of production to their points of consumption and also for their carry-over from time of production to time of use. The final result is therefore to increase greatly the supply of nutrients to the world's populations.

B. SURE

Exploration for new sources of foods, particularly those providing protein, continues to engage investigators and agencies involved in nutrition research. In addition to the suggestions offered below, the use of algae and other products is being seriously studied as a means of providing additional nutriments in certain areas of the world.

Unexploited Technological Possibilities of Making Food for Man and Animals. N. W. Pirie. *Proc. Brit Nutrition Soc.* 15: 154, 1956.

The three outstanding possibilities are: the synthesis of food, the more economical use of crops of the type we already grow, and the exploitation of new primary sources of food. One solution to the food problem would be to increase the amount grown. Even if this were done, there would still be room for improvement because much of the crop, i.e., leaves, straw, and peel, is wasted. Furthermore, the diets eaten in many parts of the world are inadequate. They have many faults but protein deficiency is a common one and the steps that could be taken to overcome it will serve as an example of what could be done to remedy the other deficiencies.

The parts of a plant generally eaten are the starch depots such as grains and tubers. Some legume seeds contain adequate amounts of protein but many tubers contain very little. Cassava with only 1 to 2 per cent is an extreme example. As would be expected from their active metabolism, immature flowers and young leaves can be rich in protein, but they are inadequately exploited.

The investigation of systems of husbandry that would ensure large yields of protein-rich and fiber-poor leaves is a technologic possibility that deserves fuller exploration. Fresh, lush leaves are pulped to an extent sufficient to release from the cells most of the free protein and protein associated with the chloroplasts and other structures. The juice that is then pressed from the mass brings these various forms of protein with it. The protein is coagulated and separated from most of the highly flavored or toxic components of the leaf by filtration.

B. SURE

Some Technological Developments of Importance in Animal Nutrition. J. Duckworth. *Proc. Brit. Nutrition Soc.* 15: 160, 1956.

One-half of the British national supply of protein concentrates was imported in 1953 and 1954. In 1955 there was a large increase in supplies, mainly of imported oilseed meals. The kinds and, particularly, the origins of imported concentrates varied greatly over the 3-year period. Little research on the nutritive value and less on local processing methods has been published from most sources of these feeding stuffs. Processing has a profound effect on the nutritive value of protein concentrates and, if inadequately controlled, yields highly variable products. Extensive research has been done only on fish, herring, soybean, and cottonseed meals. This is almost entirely from the standpoint of suiting the products to nonruminant needs. A recent trend has been to process oilseed meals for high solubility of protein. Such materials are contraindicated for ruminants under preferred British feeding systems.

Attention is now being given to developing rapid laboratory tests of protein quality. If success is attained an appropriate amendment of the Fertilizer and Feeding Stuffs Act would give protection against low-value protein concentrates of domestic or imported origin, and thus lead to more efficient compounding of rations.

B. SURE

The toxic hazards of food additives used in the preparation of various dietary items is an important area for continuing research and careful surveillance. The recent experience with lithium salts as a substitute for sodium chloride is an example of some of the dangers involved.

The Potential Toxicity of Chemicals Used in Food Technology. J. M. Barnes. *Proc. Brit. Nutrition Soc.* 15: 148, 1956.

Many of the substances used as food additives possess no outstanding toxic property. Others may be used as adjuncts in processing and may be toxic but are present in the food only in very small quantities. Food manufacturers and allied commercial interests are so aware of this problem of toxicity that it is unlikely that any material with demonstrable toxic properties will ever be included in food prepared in accordance with reputable trade practices. Compounds with well-marked toxic properties and active as insecticides, fungicides, and germicides, or endowed with other special properties may appear in food in trace quantities as the result of current practices. Every toxic substance has a dose-response curve, and below a certain dose no toxic effects can be detected. A safe dose will be one which the body can dispose of without harm to its normal metabolism.

Not only may the chemicals added to food become altered but so, too, may the food itself, and the products of such reactions might be toxic. The classic example is the agene process for "improving" flour. Can the discrepancy between the experimental observations on the dog and the apparent harmlessness of agenized flour for man be explained? Agenized flour was shown to be toxic to dogs, cats, rabbits, and ferrets. Rats and monkeys were relatively insensitive. Observations on 19 human beings including five epileptics who were given flour treated by 20 to 30 times the usual quantity of agene showed no change in behavior, general physiology, or the electroencephalogram. When the active toxic agent, methionine-sulphoximine, was isolated, the sensitivity of animals was further checked. The dose required to induce fits in the monkey is at least 100 times as great as that needed in the dog. A man eating 2,000 cal daily as agene-treated flour ingests a dose of 1 mg methionine-sulphoximine/kg. The sensitive dog requires 2 to 4 mg methionine-sulphoximine/kg to produce fits and kill the animal, but the dose-response curve must be steep, for on a diet containing up to 30 per cent of agenized flour, dogs lived in perfect health for a year and showed no electroencephalogram changes. Unfortunately, it is not yet possible to understand exactly why the dog and man differ in their sensitivity to methionine-sulphoximine. It is known that methionine in much bigger doses can counteract the effects of methionine-sulphoximine but the nature of the toxic action of methionine-sulphoximine has not been defined.

In all applied toxicologic work of this type it is difficult to overemphasize the importance of the chemist and biochemist in devising methods suitable for the detection and estimation of biologically active contaminants in such a chemically complex environment as food. Toxicity is not a specific measurable characteristic like the melting point or molecular weight of a substance. The toxicity of a substance is related to the other conditions in a living system which is exposed to its influence. Clearly, it is essential to have an accurate estimate of the quantities of any such materials that might be consumed, and if toxic effects can be demonstrated in animals, generous safety factors must be allowed before a safe dose for man can be suggested. The duty of the toxicologist must be to guide those who wish to introduce a new technical process into food production or manipulation so that they will avoid exposing the consumer to any foreseeable risk of intoxication, however mild in degree. It would seem to be the duty of those with training and experience in nutrition to advise whether or not a proposed new process has merit or possible danger on other grounds. The opinion of these experts in turn may be modified by what they learn about the possible toxic hazards involved.

B. SURE

The effect of exposure of foods to atomic blast radioactivity is a matter of considerable importance in relation to Civil Defense and the maintenance of food supplies during the present era when atomic warfare is something less than a remote possibility.

Food Supplies After A-Blast. A Report. *J. Agric. and Food Chem.* 4: 910, 1956

The Food and Drug Administration in cooperation with Federal Civil Defense exposed 100 different types of commodities, about 1,500 tons, to an A-blast in Nevada in May 1955. At one to three miles from ground zero the products were in store-type and home-like structures, and basements. The second test was set up in an area a quarter-mile from the blast; there the foods were placed in shallow trenches covered with one to two inches of earth. In the test area beyond one mile from ground zero the damage was only of a physical nature such as results from other types of explosions and hurricanes. Here all foods were considered safe for immediate consumption. Within the quarter-mile test area not only was there physical damage (glass container breakage, dented cans, split wooden panels, crushed and bruised perishables) but many of the foods were rendered unfit for consumption mainly because of induced radioactivity. Phosphorus^{32} was formed in excessive amounts in dry milk solids, cheese, butter, margarine, sea foods, and a number of other canned foods. Chlorine^{36} was also formed in salt-containing foods. Toxic compounds were not detected in any of the foods; neither were there significant losses of vitamins. Metal and glass containers became moderately radioactive, and the contents were protected in some cases. Foods from the quarter-mile test area were made into diets for rats. There was no deviation from normal growth noted in the animals even after one year. However, it is recommended that such radioactive foods be used only under extreme disaster conditions and then only for a short time. Also it is noted that relatively larger explosions of the thermonuclear type may cause still greater damage to foods.

F. E. RICE

PROTEIN METABOLISM—EXPERIMENTAL AND CLINICAL STUDIES

Perfusion experiments of the surviving liver in vitro have led to a clearer understanding of the role of this organ in protein biosynthesis, utilization of fats, carbohydrate metabolism, and steroid hormone interconversions in the hands of Dr. L. Miller and associates. The effect of insulin upon amino acid metabolism has been studied by other methods indicating increased utilization in protein formation. The liver perfusion studies reported below indicate that insulin does not produce a net increase in protein but merely an increased turnover rate of protein. The combination of growth hormone and insulin may be expected to increase protein anabolism.

Studies on Growth Hormone. I. The Effects of Growth Hormone and Insulin Upon the Synthesis of Protein in Perfused Livers. J. F. Prudden, M. K. Young, Jr., and J. A. Stirman. *J. Lab. & Clin. Med.* 47: 350, 1956.

This paper describes some studies on the effects of growth hormone and insulin upon the synthesis of protein in perfused livers. The technic is described in a previous paper (*J. Lab. & Clin. Med.* 46: 155, 1955) and will not be reviewed here other than to say that it is a complicated technic.

The authors feel that by this technic they have shown that growth hormone has an over-all anabolic effect on the protein metabolism of the perfused liver. This was primarily increased anabolism with some inhibition of catabolism. Insulin appeared to stimulate both anabolism and catabolism. The turnover rate for both hepatic and plasma proteins was more rapid under the influence of insulin. A combination of insulin and growth hormone was not as effective in increasing anabolism as was growth hormone alone.

This represents a tremendous amount of work and may prove to be an excellent way of studying the effects of hormones on protein metabolism. It should be remembered that effects on liver proteins do not mean that all proteins will be affected in a similar fashion, for example cortisone will decrease muscle protein while increasing liver protein. Confirmation of this method by others will be awaited with much interest.

K. R. CRISPELL

In the geriatric patient, impaired nutrition has often been ascribed to the lack of taste for protein foods and preference for easily consumed carbohydrate foods. The absorption of protein is not reduced in aging patients.

Studies of Protein Absorption Using Nitrogen^{15} as a Tag. G. S. Sharp, S. Lassen, S. Shankman, A. F. Gebhart, Jr., and J. W. Hazlet. *J. Nutrition* 58: 443, 1956.

Increasing interest is found in the literature concerning the assimilation and utilization of protein foods as one of the major deficits of the geriatric patient. However, a marked decrease in utilization capacity, as a function of age alone, has not been reported in well-controlled studies.

Methods for the study of protein absorption in man have been discussed. A yeast-protein tag with an N^{15} content of 58.3 atom per cent excess was prepared. Evidence for the general distribution of the tag throughout the protein fraction of the yeast has been reviewed. A mean yeast-protein absorption of 90.3 per cent among six subjects has been determined. Achlorhydria, hypochlorhydria, and age do not appear to produce depressing effects on the capacity to absorb a protein tracer during continued high-level protein intake. The single dose tracer method of determining protein absorption has been shown to obviate the need for evaluation of endogenous nitrogen. B. SURE

The biologic value of protein has been analyzed by bioassay methods such as growth rates of animals. The chemical analysis of protein for its amino acid constituents may also provide a reliable means of determining the potential nutritional value of these foods.

Measurement of the Net Utilization of Heat-Processed Proteins by Means of the Pepsin Digest-Residue (PDR) Amino Acid Index. A. L. Sheffner, R. Adachi, and H. Spector. *J. Nutrition* 60: 507, 1956.

It has long been recognized that the nutritional value of a protein is dependent primarily upon its constituent amino acids. Nevertheless, only since the publication in recent years of reliable and relatively simple methods for amino acid analysis has it been feasible to develop *in vitro* procedures for the measurement of protein quality. These procedures, based upon chemical analysis of proteins for their essential amino acids, yielded figures which were well correlated with biological values.

The pepsin digest-residue (PDR) amino acid index was found to reflect the effects of heat processing upon the net protein utilization of proteins and mixed protein foods. Data are also presented which indicate that the discrepancy between the PDR index and the net utilization value of raw soybean meal is due to the presence in raw soybeans of substances which exert effects apparently unrelated to the enzymatic release of amino acids. The PDR index can be used to predict the net utilization of soybean meals accurately if these "toxic" factors are inactivated. B. SURE

Studies on normal levels of serum protein in children from infancy to puberty show a decline after birth with a return to adult levels after a variable period. The postnatal drop in the protein fractions may be due to less favorable conditions for protein synthesis immediately after birth or to the loss of transplacental circulation of protein to the fetus.

Electrophoretic Analysis of Serum Proteins in Infants and Children. J. W. Oberman, K. O. Gregory, F. G. Burke, S. Ross, and E. C. Rice. *New England J. Med.* 255: 743, 1956.

Little data exist regarding the normal range of serum protein levels in healthy infants and young children. The little there is was compiled, for the most part, before the time of paper electrophoresis. Serum from 159 children, ranging in age from the newborn to 13 years, was analyzed for this study, using paper electrophoresis.

Total protein was found to be lower in the cord blood of new born infants than in their mothers at term. Adult levels were reached at one to two years of age, though the mean values of three to four month old children fell within the observed adult range.

Serum albumin levels were lower in mothers at term and in their newborn infants than in normal adults. After the child reached three months of age the levels did not differ from that of an adult. The level of serum albumin was somewhat greater in children 6 to 13 years of age. This gives greater values for total protein.

The total globulin levels were much lower in the newborn infant than in mothers at term. There was a steady fall in serum globulin until the third or fourth

month with a slow rise thereafter until adult levels are reached at seven to eleven months. The rise in total serum globulin and its gamma fraction found when a child was three to five years old was probably due to the increased exposure to infection.

Alpha globulin serum levels were somewhat higher in mothers at term than in the newborn infant. The α_1 globulin fell slightly until the child was three to four months of age though the average levels did not vary much throughout all ages. The lowest values of α_2 globulin were reached during the first week of life, then rose to a stable mean. At seven to eleven months of age the highest levels of α globulin were reached after which there was a decrease with increasing age. Compensating for the falling level of gamma globulin after birth there was a rise in β globulin. The level of β globulin was higher in mothers at term than in their newborn infants. After the rise in β globulin the mean percentage of β globulin remained fairly constant throughout childhood.

There was no difference between serum gamma globulin levels in the newborn infant and the mother at term. The level of gamma globulin of the infant fell steadily until it reached its lowest point in a child three to four months of age. There was then a slow increase until the age of three to five years when the level was the same as that of an adult. M. W. BATES

Extravascular phase albumin held in areas of abnormal fluid accumulation such as ascites or edema is not rapidly equilibrated with circulating albumin. Measurement of the turnover time of the extravascular albumin is necessary and may be found to vary considerably in different sites of fluid retention.

The Persistence in the Blood of the Radioactive Label of Albumins, Gamma Globulins, and Globulins of Intermediate Mobility. IV. Specific Activity Ratios Between Plasma and Edema Fluid of I-131-Labeled Albumin Injected Intravenously in Nutritional and Nephrotic Hypoproteinemia. D. S. Kushner, D. Bronsky, A. Dubin, B. Maduros, and S. H. Armstrong, Jr. *J. Lab. & Clin. Med.* 49: 440, 1957.

In three patients with hypoalbuminemic edema (one nephrotic, two nutritional) the specific activity of edema and urine albumin was compared with that of contemporaneously obtained serum albumin following intravenous injection of I^{131} labeled albumin.

The apparent time for turnover of albumin from all sources was found to be markedly shortened and total exchangeable albumin pools were reduced to about a quarter of the normal range.

In one patient the turnover time for edema albumin was much prolonged compared to serum albumin. This suggested a failure of equilibration between extra- and intravascular albumin due perhaps to a "trapping of some of the labeled protein beyond the reach of the metabolic processes to which serum albumin is injected." The findings are discussed in terms of some of the difficulties of interpretation involved in apparent turnover time and exchangeable pool estimates from extrapolation of radioactivity die-away plots.

This is a very interesting study and raises many questions about previous similar types of studies. This is particularly true in patients who are not in the "steady state." K. R. CRISPELL

Conversion of protein to glucose proceeds through deamination of the amino acid components of the digested protein and gluconeogenesis of deaminated residues. This circuitous route of glucose formation results in little change in blood glucose values under normal conditions.

Effect of Proteins on the Blood Glucose Levels. G. Joachimoglu and H. N. Antoniades. *Diabetes* 5: 383, 1956.

The authors present studies on the changes in level of blood glucose, after feeding normal and diabetic human subjects with various amounts of isolated plant proteins, gelatin, and egg white. Eighty normal and eight diabetic volunteers were the subjects of the study. A total number of 176 experiments were performed studying the effect of whole egg white, gelatin, and proteins prepared from lentil, oat, wheat, and pea bean.

An increase of glucose in the blood was determined at three and one-half and five hours following the ingestion of the different proteins. The data suggest that egg albumin has the highest rate of conversion to glucose, followed by oat, wheat flour, lentil, and pea bean proteins. K. R. CRISPELL

Rapid disappearance of injected labeled human albumin in a patient with hypoproteinemia may reflect an increased rate of utilization of the protein for replenishment of depleted tissue protein reserves rather than a hypercatabolic state as described below.

Idiopathic or Hypercatabolic Hypoproteinaemia. Case Examined by I^{131}-Labelled Albumin. M. Schwartz, and B. Thomsen. *Lancet* 1: 14, 1957.

In some persons with a low serum-protein level, no disease process can be found to explain it and this condition has been termed idiopathic hypoproteinemia. A case is described in detail of a 25-year-old woman with this condition. She was investigated by injecting 30 mg of I^{131}-labeled pure human albumin and studying its disappearance from the serum. The half life of the labeled protein was about seven days compared to about 22 days for a normal woman. The authors conclude that the basic defect in this condition is one of hypercatabolism and they suggest the name hypercatabolic hypoproteinemia. F. E. HYTTEN

Protein malnutrition may be due to many primary or secondary factors in the human. Studies from various countries where the condition is common reveal a variety of clinical patterns depending upon the type of diet consumed and the presence or absence of parasitic infestation.

Protein Malnutrition in Brazil. J. Waterlow and A. Verguia. *Bull. World Health Organ.* 15: 165, 1956.

A survey of protein malnutrition in Brazil was conducted in five major cities. The condition known also as kwashiorkor or pluricarencial dystrophy is prevalent in certain regions among children two to three years old and where one-third of them are undernourished. With no exception, all of the patients suffered from parasitism, especially ascaridiasis. In contrast with African kwashiorkor, liver cirrhosis is uncommon. Dried skimmed milk was the therapy used satisfactorily. Mortality is high, at 20 to 30 per cent. S. O. WAIFE

The relative constancy of the desoxyribonucleic acid content of the cells provides an index for the determination of other cellular constituents under various metabolic conditions.

Use of Desoxyribonucleic Acid as a Reference Standard in Metabolic Experiments. D. E. Gray and H. A. Deluca. *Am. J. Physiol.* 184: 301, 1956.

The metabolic activity (as gauged by glycogen synthesis, glucose uptake, and oxygen consumption per gram of wet tissue) was found to be increased in diaphragms taken from rats maintained on a low-protein diet compared to normal controls. There was no significant difference in these indices of metabolic activity when they were expressed on a per cell basis (calculated on the content of desoxyribonucleic acid phosphorus). In protein deprivation, the mass of the diaphragm cell was dependent upon the protein intake rather than the total caloric intake but the metabolic activity of the cell was independent of its mass. These findings suggest that the metabolic activity of a tissue may, under certain experimental conditions, be more suitably expressed on a per cell basis than on the more usual basis of wet weight of tissue. AUTHORS

The following abstracts deal with several aspects of protein metabolism in experimental animals.

Role of Urea in Rat Proteinuria. J. S. Finlayson and C. A. Baumann. *Am. J. Physiol.* 184: 469, 1956.

Dietary casein and soy protein were equally effective in increasing the normal proteinuria of the male rat. Urea fed *ad libitum* increased proteinuria, but the increase was usually less than that due to an isonitrogenous level of casein. Urea fed 2 hr/day brought on a rapid increase in proteinuria, which over the rest of the day followed neither the blood levels of urea nor the intake of water. An amino acid mixture, prepared to imitate the composition of casein increased proteinuria to that caused by an isonitrogenous addition of urea but less than that caused by an equivalent high-protein diet. Varying the level of vitamin B_6 had no effect on the proteinuria of rats on several different diets. A simplified method for the routine estimation of rat urinary protein by centrifugation is presented. AUTHORS

Role of Dietary Protein in Normal Rat Proteinuria. H. W. Rumsfeld, Jr. *Am. J. Physiol.* 184: 473, 1956.

A twofold increase in proteinuria, which is produced by raising the dietary content of casein from 12 or 18 per cent to a level of 50 per cent was duplicated by other proteins fed either singly or in combinations. The type of urinary protein was not electrophoretically altered by the protein fed. Increased urea and water excretion, common factor associated with the intake of the various proteins, were investigated. Urea, either fed or injected, was found to cause a proteinuria similar in many respects to that produced by intact protein. Water loading experiments separated the two factors to show that a much closer parallelism exists between urea and protein excretion than between the latter and urine volume. AUTHORS

The Nitrogen Balance of Pregnant Rats. S. D. Morrison. *J. Physiol.* 133: 167, 1956.

These studies demonstrate that during the last week of pregnancy food intake decreases to about 65 per cent of that established during the period of gestation previous to the terminal seven days. However, the nitrogen balance remains positive during this last week. There may be a decline to or approaching negative values from the fourth day antepartum. Positive values are resumed immediately after this. There is a more rapid decrease in urinary nitrogen excretion (during the period of reduced food intake) of pregnant rats than in nongravid rats. This last observation is probably responsible for the positive nitrogen balance in the face of reduced ingestion of food.

M. J. OPPENHEIMER

Action of the Hypophysis and of Dietary Protein on the Calcifying Tissues. J. T. Irving. *Nature* 178: 1231, 1956.

It is known that protein deficiency interferes with endochondral calcification in growing rats, and similar changes, together with very marked changes in the teeth, have been described after hypophysectomy. It has been felt by some that these two effects were connected.

In the present experiments young growing rats were given diets containing 9.3 per cent protein for from 10 to 117 days. Marked bone changes occurred and these could be prevented by raising the protein content to 18.8 per cent. There were no abnormalities of the teeth. It is concluded that the fundamental action of the hypophysis and of protein on the hard tissues must be completely unconnected.

F. E. HYTTEN

The Importance of Protein Metabolism and Liver Function in Geriatric Surgical Patients. J. H. Schneewind, J. B. Fuller, and W. H. Cole. *J. Am. Geriatrics Soc.* 5: 1, 1957.

The authors present data from the histories of four elderly patients which they feel indicate the need for careful evaluation of nutrition, protein reserve, and liver function prior to operation.

The data are presented in an uncritical fashion and add confusion rather than clarification to the problem of surgery in the geriatric patient. K. R. CRISPELL

ITEMS OF GENERAL INTEREST

Histochemical Studies on the Cerebral Lipoidoses and Other Cellular Metabolic Disorders. B. H. Landing and D. G. Freiman. *Am. J. Pathol.* 33: 1, 1957.

The nature of the lipid found in nerve cells of lipid storage diseases, non-lipid histiocytosis and Werdnig-Hoffmann's infantile muscle atrophy was studied. Except for the latter disease the nerve cells affected in the various disorders contained protein-bound lipids insoluble in organic solvents after fixation in formalin. Even though ten different histochemical stains were used, it seems impossible at present to go beyond the statement that all these diseases are associated with the occurrence of sphingolipids in the nerve cells. No distinction can be made between the different types of sphingolipids. The *in vitro* tests on purified lipids in an analysis of the staining properties of the intracellular lipoproteins were found to be unreliable.

M. SILBERBERG

Lactose as a Lipotropic Agent. D. P. Sadhu. *Nature* 177: 1236, 1956.

Addition of lactose to the diets of young albino rats increases their food intake; they grow better than control rats fed on sucrose. In the experiment reported here, four groups of 12 albino rats were used. One group received a full diet containing 58 per cent sucrose and no lactose; the others received the same diet in which 10, 20, and 30 per cent of the sucrose was replaced by lactose, for four weeks. The choline and phospholipid content of the liver and kidney rose as the lactose content of the diet rose; the fat and sphingomyelin fell.

"This has an important bearing on the kwashiorkor syndrome, where lack of milk and absence of lactose in the diet of the young after early weaning may be responsible for the fatty liver, which is caused as a result of the lack of choline sparing and lipotrophic effects of lactose." F. E. HYTTEN

Thermochemical Efficiency of Growth in Rats. J. Mayer and J. Vitale. *Am. J. Physiol.* 189: 39, 1957.

A simultaneous study of changes in food intake and body composition during the three months of postweaning growth was undertaken on three large groups of albino rats fed semi-synthetic diets containing, respectively, 10, 25, and 60 per cent protein. The results show a remarkable similarity of percentage of body weight represented by protein during the whole growth period for the three groups and constancy within each group. The thermochemical efficiency (ratio of calories deposited to calories ingested) was constant from weaning to puberty and particularly so on the diet with the protein content most favorable for growth (25 per cent). The thermochemical efficiency, ratio of calories deposited to calories ingested, was approximately constant from weaning to puberty, on optimal diets and high-protein diets, declined somewhat earlier on a low-protein diet. AUTHORS

Erythrocyte Turnover in Rats Fed Diets High in Methionine. H. P. Cohen and C. P. Berg. *J. Biol. Chem.* 222: 85, 1956.

It was noticed that feeding high concentrations of methionine to young rats induced deposition of iron in the form of hemosiderin in the spleen. Reticulocyte and erythrocyte counts and hemoglobin were normal.

It was therefore felt that deposition of hemosiderin might occur without noticeable anemia, provided that the turnover rate of the red cells was increased. To check the turnover rate of erythrocytes in rats fed high-methionine diets and rats fed normal diets, the animals were injected with glycine-2-C^{14} to produce radioactive hemoglobin. The red cells of the former rats showed a more rapid increase in radioactivity, followed by a more rapid decrease. Hence it was concluded that excess dietary methionine accelerates erythrocyte (hemoglobin) turnover, at the same time making it possible for hemosiderin to be deposited in the absence of anemia.

M. K. HORWITT

Some Pediatric Implications of the Vanderbilt Cooperative Study of Maternal and Infant Nutrition. C. W. Woodruff, E. B. Bridgeforth, M. P. Martin, W. J. McGanity, and W. J. Darby. *Am. J. Dis. Child.* 90: 595, 1955 (Soc. Trans.).

The Vanderbilt Cooperative Study of Maternal and Infant Nutrition includes appraisals of dietary intake, nutritional physical evaluations, and biochemical assessments of nutriture once each trimester and six weeks post partum. Independent appraisals of clinical performance of mothers and infants were made. Over 2,000 consecutive admissions to the prenatal clinic during 1945 to 1949 are included.

This report relates the performance of the infants to maternal nutriture. The relation of birth weight to maternal size is considered in comparisons including birth weight. No relationship to maternal caloric or protein intake was found.

The mothers of premature infants present a pattern of relative underweight, higher hemoglobin concentrations in the third trimester, and lower vitamin C intakes and serum ascorbic acid levels than do the mothers of full-term infants.

Congenital malformations occurred in 2.6 per cent of

the infants. A search for associated deviations in the nutriture of their mothers was entirely negative.

The hemoglobin concentration of the infant at birth and at the age of six weeks showed no variations which could be related to the nutritional status of the mothers.

The nutritional level of these mothers is above that at which it becomes the determining factor in these pediatric complications. Consequently, attempts to reduce the incidence of these complications should be directed toward investigating their etiology rather than supplementing the diets of the mothers.

J. N. ETTELDORF

Influence of Vitamins Upon Some Teratogenic Effects of Radiation. D. H. M. Woollam, C. W. M. Pratt, and J. A. F. Fozzard. *Brit. Med. J.* 1: 1219, 1957.

The effect of vitamin administration on the teratogenic effects of x-radiation was studied in pregnant white rats. Two groups of rats received a dose of x-rays of about 258 r and two groups received none. One group of each pair received 10,000 units of vitamin A; 50,000 IU of vitamin D; 60 mg α-tocopterol acetate; 70 mg thiamine; 45 mg nicotinamide; 1 mg riboflavin; 15 mg pyridoxine; 1.5 mg calcium pantothenate; 40 mg benzyl alcohol and 150 mg of sodium ascorbate.

There were no deformed fetuses in the two groups which received no radiation. Both radiated groups however, had a high incidence of deformity (anophthalmia, micropthalmia and hydrocephalus) but the incidence was considerably greater in the group which received vitamins and radiation. For example, the vitamin-fed group had an incidence of 37.4 per cent anophthalmia compared to an incidence of 10.8 per cent in the group receiving radiation alone. It is suggested that the effect of the vitamins is to sensitize the cells of the developing eye to the destructive action of radiation.

F. E. HYTTEN

Intestinal Sterols. III. Effect of Age, Sex and Diet. D. Coleman and C. A. Baumann. *Arch. Biochem.* 66: 226, 1957.

Cholesterol, 7-dehydrocholestenol, cholestanol, "sterol D," and coprostanol contents were determined in feces of rats fed on a synthetic fat-free diet. The daily excretion in adult male rats averaged 1.5 mg of dehydrocholestenol, 0.97 mg of cholesterol, 0.45 mg of cholestanol, 1.48 mg of "sterol D" and 5.7 mg of coprostanol. Male rats excreted more sterols than females, and castrates excreted less than either with the exception of coprostanol. Sterol excretion increased with age, especially in males, and there was a considerable increase in the unsaturated or 7-dehydrosterols as compared with cholesterol. Dietary penicillin and sulfasuxidine depressed the excretion of coprostanol, while excretion of cholesterol was increased by penicillin. Aureomycin, streptomycin, and chloromycetin had no effect on sterol excretion. The addition of up to 5 per cent cellulose to the fat-free diet led to moderate increases in the excretion of all sterols to approximately the same extent. The feeding of 0.2 to 0.5 per cent cholesterol increased the excretion of cholestanol and coprostanol as well as the cholesterol itself. The ingestion of 0.5 per cent 4-dehydrocholestenone caused moderate increases in all of the sterols tested and appeared to be easily converted in the intestine. Ingestion of 7-dehydrocholestenol only increased the excretion of the fed sterol, indicating that the 7-dehydrosterol is not readily converted to cholesterol or coprostanol in the intestine. The inclusion of 20 per cent lard in the diet did not cause any changes in sterol excretion.

M. K. HORWITT

Nutritional Evaluation of Coffee Including Niacin Bioassay. L. J. Tepley and R. F. Prier. *J. Agric. and Food Chem.* 5: 375, 1957.

Samples of retail coffee were found to contain from 7.4 to 11.0 mg niacin per 100 g of coffee. Most of the niacin is readily extracted in making the beverage. It is estimated that a cup of beverage may contain about 1 mg of niacin, and that 3.5 cups per day could supply about one third of the daily minimum requirement. "The niacin supplement from coffee might be important to certain individuals." Moderate amounts of extractable calcium and iron were found present, and low levels of other B vitamins and fluorine. F. E. RICE

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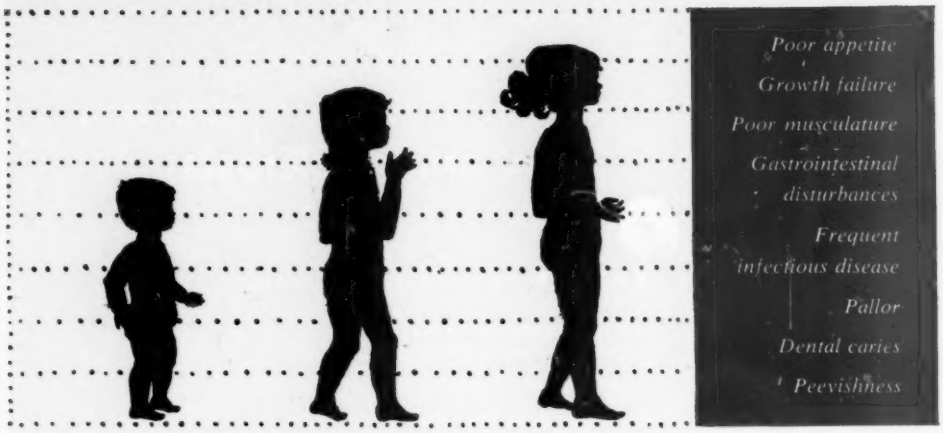

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THE ROLE OF PROTEIN IN DIETS FOR WEIGHT REDUCTION
Vincent P. Dole 591

In this important paper, Doctor Dole shows that a calorically restricted but balanced diet is effective in the treatment of obesity. Moreover, the concept that loss of nitrogen may be a proper part of weight reduction has widespread implications. This thoughtful analysis deserves careful consideration.

TOCOPHEROL EXCESS IN MAN. CREATINURIA ASSOCIATED WITH PROLONGED INGESTION
Robert W. Hillman 597

In this unusual investigation, a normal volunteer ingested vitamin E in excess for 93 days. The results, especially with respect to creatinuria, are significant in adding to our understanding of the metabolic role of the tocopherols. Clearly, more studies of this type are needed.

A FORMULA FOR ESTIMATING THE SPECIFIC GRAVITY OF THE HUMAN BODY WITH A CONSIDERATION OF ITS POSSIBLE USES
George R. Cowgill 601

This study, by a distinguished scientist, is an important addition to our knowledge of "nutritional anthropology." By devising a practical formula for the estimation of specific gravity from height and weight, Doctor Cowgill has given us a useful tool for further investigation relating to body composition.

THE ROLE OF NUTRITIONAL FACTORS IN THE CAUSE, PREVENTION, AND CURE OF ALCOHOLISM AND ASSOCIATED INFIRMITIES
Robert S. Goodhart 612

In a concise review of a complex subject the author summarizes the salient points in our knowledge of nutrition and alcoholism. He also indicates those areas in which our information is inadequate; all in all an excellent review of a much discussed subject.

THE LOW-SODIUM DIET. SOME METHODS OF MAKING IT MORE ACCEPTABLE WITH SPECIAL REFERENCE TO THE USE OF BITTERS
Milton Plotz 618

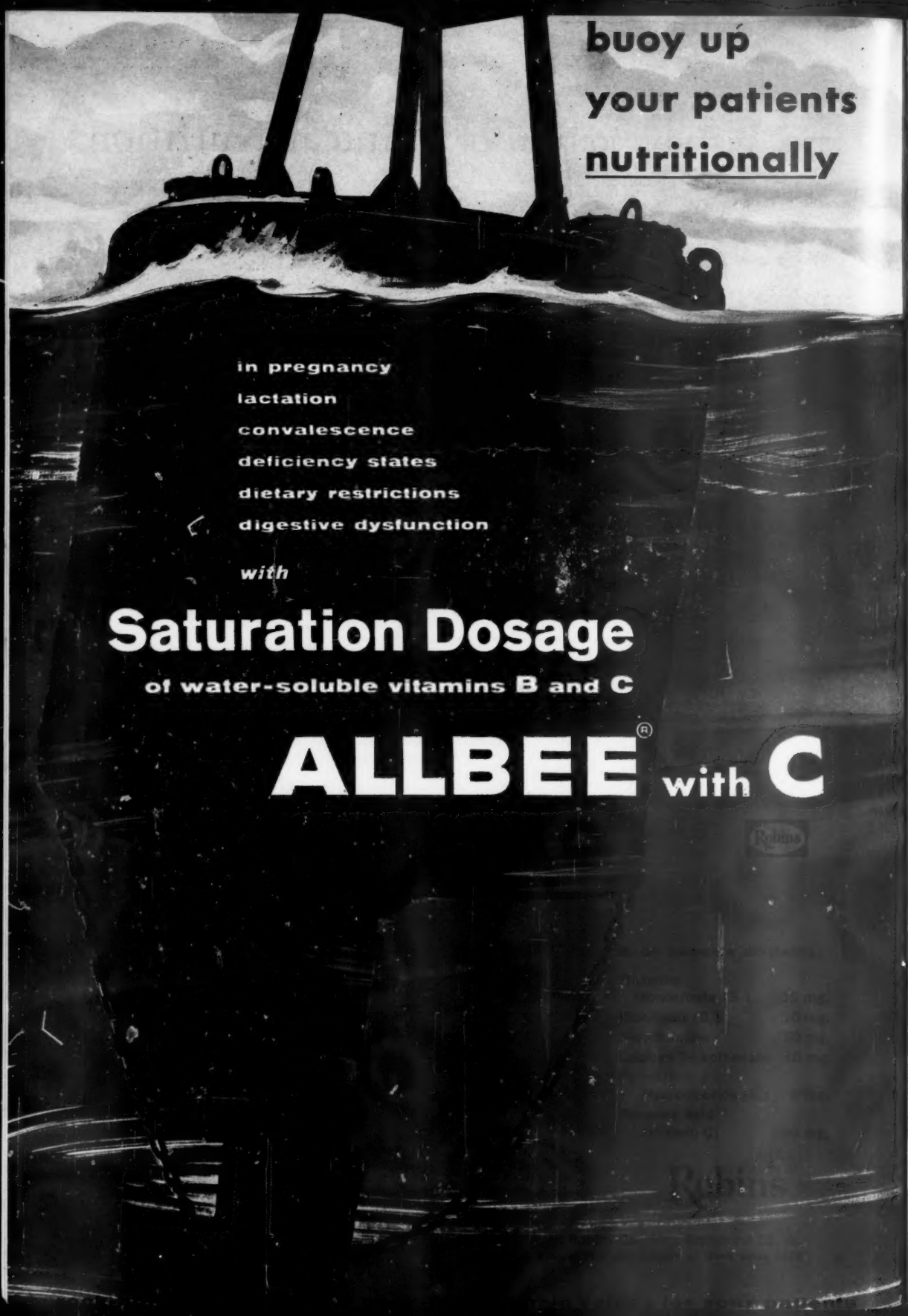
The simple procedures described in this clinical report will go a long way in making low-sodium diets more acceptable to the patient. Everyone who deals with this common situation will appreciate the significance of the paper.

EFFECTS OF IRON TREATMENT OF ANEMIA IN A TROPICAL AREA
P. L. White, A. Quiroz, L. Gonzales-Mugaburu, S. Morales, J. Atkins, C. Collazos, and D. M. Hegsted 621

Anemia is common among population groups suffering from various parasitic infestations. This cooperative study describes a clinical experiment with iron supplementation. The public health aspects of this subject are of major importance.

SERUM CHOLESTEROL LEVELS IN SCHOOL CHILDREN FROM THREE SOCIO-ECONOMIC GROUPS
Nevin S. Scrimshaw, Alan Balsam, and Guillermo Arroyave 629

This paper reports the results of a study to determine the total serum cholesterol levels of schoolchildren from various socio-economic groups. The findings presented show significant differences between these groups. Age and sex have no bearing on these variations. This represents an important contribution in helping to clarify this controversial subject.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DIETARY SURVEY ON RARATONGA, COOK ISLANDS. III. FEEDING PRACTICES AND GROWTH OF RARATONGAN CHILDREN FROM BIRTH THROUGH SIX YEARS Peggy Crooke Fry 634

Concluding a three-part survey of nutritional-anthropologic interrelations among Polynesians, this paper indicates how social factors affect the growth and development of the young. Studies of this type are rare and the information they supply, unique.

A SYNDROME OF OSTEOPOROSIS IN AFRICANS AND ITS RELATIONSHIP TO SCURVY H. Grusin, and E. Samuel 644

The Johannesburg school of clinical nutritionists have made many important contributions to our fund of nutritional knowledge. In this excellent clinical study of osteoporosis the significant observation of the possible role of vitamin C is described. These findings may open up new areas of research.

THE EFFECT OF INTRINSIC FACTOR ON THE ABSORPTION OF VITAMIN B_{12} IN OLDER PEOPLE
Stanley M. Chernish, Oscar M. Helmer, Paul J. Fouts, and Kenneth G. Kohlstaedt 651

Using both plasma levels and urinary excretion studies the metabolism of vitamin B_{12} was studied in middle aged and elderly people residing in a County Home. The findings indicate not only that plasma level declines with aging, but that a few non-pernicious-anemia patients may have deficient absorption which can be corrected by the oral administration of intrinsic factor concentrates. This is further evidence that the nutritional needs of the elderly are an important and poorly understood problem.

DR. A. J. CARLSON AND THE CONCEPT OF HUNGER Frederick Hoelzel 659

The long-time associate and co-worker of A. J. Carlson gives us an intimate view of the development of Carlson's concept of hunger and appetite. Seen through the eyes of an active participant in a major contribution to physiology, this account will be of interest to students of all disciplines.

HEREDITARY FACTORS IN PROTEIN NUTRITION Paul F. Fenton 663

Experimental data are presented showing that hereditary factors are involved in groups of animals having significantly different metabolic patterns. From studies of this type will come a better understanding of individuality in nutrition.

RELATION OF VITAMIN A DEFICIENCY AND ESTROGEN TO INDUCTION OF KERATINIZING METAPLASIA IN THE UTERUS OF THE RAT
Walter J. Bo 666

Interrelationships between hormones and vitamins are clearly shown in this experimental study. Both avitaminosis A and hyperestrogenism may produce a keratinizing metaplasia of uterine epithelium. This paper reports further investigations along these lines.

EDITORIAL: DIET AND ATHEROSCLEROSIS—THE EVIDENCE FROM ISRAEL William Dock 674

DIET THERAPY: ADAPTING THERAPEUTIC DIETS TO JEWISH FOOD CUSTOMS
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ABSTRACTS OF CURRENT LITERATURE: Potassium Metabolism; Fats and Coagulability of Blood; Nutritional Value of Lysine Supplementation; Food Technology; Protein Metabolism—Experimental and Clinical Studies; Items of General Interest . . 687

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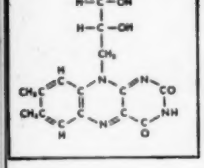
The Vital Story o

A Quick History. Independent investigators, working separately to unlock several of nature's doors, sometimes open up unsuspected relationships. This happened with vitamin B_2.

Investigations. About 25 years ago, several groups, notably Warburg's, were investigating a "yellow enzyme" obtained from yeast. Almost simultaneously other investigators were studying a food factor that aided growth of laboratory animals.

What they found. Proceeding with chemical analysis of this growth factor, the team of Kuhn, György, and Wagner-Jauregg noted a relationship between the growth-producing agent and the "yellow enzyme." Their findings, and those of other researchers along similar lines, were published in 1933. Eventually, riboflavin and an essential part of the yellow enzyme were found to be identical and the unity of an essential nutrient and cellular metabolism was established.



Isolation of pure riboflavin was achieved by Kuhn and his co-workers, and by Ellinger and Koschara, in 1933.

Nomenclature. Known in the United States as riboflavin, this vitamin has also been called lactoflavin, ovoflavin, hepatoflavin, and vitamin G.

SYNTHESIS

By 1935, two eminent chemists, working separately, had synthesized riboflavin, practically in a dead heat. Prof. Paul Karrer of the University of Zurich, a collaborator of the Hoffmann-La Roche Laboratories, produced the first successful synthesis. Five weeks later Richard Kuhn of Germany announced his synthesis of the vitamin. Prof. Karrer subsequently shared the Nobel Prize in Chemistry for his work in vitamins and carotenoids.

The Karrer synthesis forms the basis for chemical processes in widespread use today by Hoffmann-La Roche and other leading manufacturers throughout the world. Riboflavin is also manufactured today by fermentation methods.

CHEMICAL AND PHYSICAL PROPERTIES

Riboflavin is yellow, slightly water-soluble with a greenish fluorescence and a bitter taste. Its empirical formula is $C_{17}H_{20}N_4O_6$. Vitamin B_2 produced by the Roche process is identical in every way with that occurring in nature.

How does vitamin B_2 work? Riboflavin is a vital part of nature's chain of reactions for utilization of carbohydrate energy. It has been found to be a constituent of many enzyme systems and is thus intimately connected with life processes. It is probably required by the metabolic processes of every animal and bird as well as by many fishes, insects and lower forms of life. (In certain animals, however, the requirement may be synthesized by bacteria within the intestine.)

In the cells riboflavin goes to work attached to a phosphate group. This substance, known as riboflavin-5′-phosphate or flavin mononucleotide, may in turn be attached to still another essential substance, adenylic acid, forming flavin adenine dinucleotide. Either nucleotide then is attached to protein, thereby forming an enzyme, and takes its part in oxidation-reduction reactions.

Requirements in Human Nutrition. As we have seen, vitamin B_2 is essential to life. We have no special storage organs in our bodies for this vitamin, although a certain level is maintained in various tissues, with relatively large amounts found in the liver and kidneys.

MEASURING METHODS

In the beginning, riboflavin activity was described in "Bourquin-Sherman units" and requirements were thought to be very small. Subsequent research showed otherwise. Milligrams of weight became the unit and the Food & Drug Administration of the U. S. Dept. of Health, Education & Welfare has established a minimum daily requirement of 2.0 mg. of riboflavin for all persons 12 or more years old. For infants it is 0.5 mg. These requirements are designed to prevent the occurrence of symptoms of riboflavin deficiency disease. The minimum daily requirement for this vitamin for children from 1 to 12 years has not been established by the F. & D. A.

Recommended allowances. The Food & Nutrition Board of the National Research Council has recommended the following daily dietary allowances of riboflavin, expressed as milligrams. These are designed to maintain good nutrition of healthy persons in the U. S. A.

			Boys	Girls
Men			1.6	
Women			1.4	
"	(3rd trimester of pregnancy)		2.0	
"	(Lactating)		2.5	
Infants,	1-3	months	0.4	
"	4-9	"	0.7	
"	10-12	"	0.9	
Children,	1-3	years	1.0	
"	4-6	"	1.2	
"	7-9	"	1.5	
Adolescents,	10-12	years	1.8	1.8
"	13-15	"	2.1	2.0
"	16-20	"	2.5	1.9

# of VITAMIN B_2

(Riboflavin)

by Science Writer

Deficiencies of vitamin B_2 appear in several ways in human beings. The eyes, the skin, the nerves, and the blood show the effects of too little riboflavin. Laboratory animals have demonstrated that a riboflavin-deficient diet can cause death of adults and can slow or stop growth in the young. Female animals, deprived of riboflavin in the diet, may produce offspring with congenital malformations.

Medical uses. To overcome and control deficiencies in human beings, physicians have pure riboflavin available for administration by injection or orally, by itself or with other "B" vitamins or multi-vitamin-mineral combinations.

How do we get our daily riboflavin? Vitamin B_2 has wide distribution throughout the entire animal and vegetable kingdoms. Good sources are milk and its products, eggs, meats, legumes, green leaves and buds. Whole-grain cereals have significant but not large amounts of riboflavin.

ADDITION TO FOODS

Cereal foods play a large part in our diet. To produce the white flour almost all of us want, millers are obliged to remove parts of the wheat that contain much of the grain's riboflavin and other nutrients. In addition, cereal grains are not rich sources of riboflavin. Millers meet this problem by *enriching* the grain foods for which federal standards exist with vitamins B_1, B_2, niacin and the mineral iron. In the case of vitamin B_2, however, they do more than *restore* the processed food to its natural riboflavin level; they *fortify* the food with enough of this essential vitamin to make it nutritionally more valuable than it was in nature.

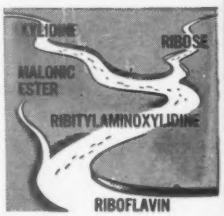
Acting to protect the good health of millions of Americans, bakers and millers adopted *enrichment* of white bread and white flour in 1941. Since that time, other foods, such as macaroni products, corn meal and grits, farina, pastina and breakfast cereals have had their food value increased by enrichment with pure riboflavin and other vitamins and minerals.

When enriching, fortifying or restoring, food manufacturers add the necessary quantity of riboflavin (and other vitamins and minerals) to the food during processing, so that the finished product meets federal, state, and territorial requirements or contributes to the consumer an amount of the vitamin that dietary experts believe significantly useful.

PRODUCTION

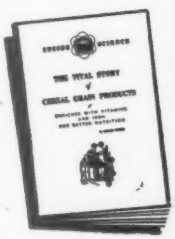
Prof. Karrer's synthesis of riboflavin was a laboratory success. Adapting the process to commercial production, however, demanded original thinking by chemists at Hoffmann-La Roche. The production of riboflavin by chemical synthesis requires the production of ribose, a rare sugar, at an early stage in the process. This special sugar must be made inexpensively if the synthesis is to be practical. Sugar chemistry is a difficult matter. In a brilliant piece of work, the Roche chemical experts developed a method to produce ribose on a commercial scale by an electrolytic process, thus overcoming a most troublesome problem. Subsequently, Roche chemists developed the first practical synthesis for riboflavin-5′-phosphate, identical with natural flavin mononucleotide.

Picture three streams joining to form a river and you have a simplified idea of the Roche process for synthesizing vitamin B_2. O-xylene and glucose are processed separately to form xylidine and ribose respectively. These are joined to form ribitylxylidine, which is then converted to ribitylaminoxylidine. Starting separately with malonic ester, which is processed through intermediate stages to alloxan, the third "stream" is then joined with ribitylaminoxylidine to form riboflavin. Purification occurs at each step of the synthesis. Riboflavin Roche* equals or exceeds U. S. P. standards.



By the tons. So efficient is the Roche process that pure riboflavin is produced *by the tons* for use in pharmaceutical products and processed foods. An interesting development by Roche is the production of riboflavin in different forms related to the method of end use. Roche*Regular riboflavin U. S. P. is especially useful in dry enrichment premixes, powdered dietary supplements, pharmaceutical tablets and soft-gelatin capsules. Roche*Solutions type is preferred for the manufacture of solutions having low concentration. Roche* Riboflavin-5′-Phosphate Sodium is a highly and rapidly soluble riboflavin compound favored for all pharmaceutical liquid products and some tablets, lozenges, and capsules. It has a more pleasant taste than the bitter U. S. P. riboflavin.

This article is published in the interests of pharmaceutical manufacturers, and of food processors who make their good foods better using pure riboflavin Roche. *Reprints of this and others in the series will be supplied on request without charge. Also available without cost is a brochure describing the enrichment or fortification of cereal grain products with essential vitamins and minerals. These articles and the brochure have been found most helpful as sources of accurate information in brief form. Teachers especially find them useful in education. Regardless of your occupation, feel free to write for them. Vitamin Division, Hoffmann-La Roche Inc., Nutley 10, New Jersey. In Canada: Hoffmann-La Roche Ltd., 1956 Bourdon St., St. Laurent, P. Q.



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FILMS

FREE UPON REQUEST

The following list of films which are available from advertisers has been compiled from various sources. Interested readers should write to the addresses listed below for additional information—Ed.

THE GOLDEN APPLE—non-technical—16 mm.—color and sound—25 minutes.

Introduced with the mythologic tale of The Golden Apple, this film traces the life-cycle of the orange from the time of its growth through its early uses in the prevention of scurvy. It presents the discovery and isolation of Vitamin C and of Hesperidin, their dietary uses, and the merging of the two into the single preparation, Bioflavonoids. The uses of Bioflavonoids in the treatment of diseases involving the capillary system are demonstrated through laboratory and clinical material. Film was produced by the National Drug Co., Philadelphia 44, Pa.

IT'S ALL IN KNOWING HOW—non-technical—16 mm. sound—Kodachrome—13 1/2 minutes

Suitable for high school and adult groups. The film uses a combination of story and animated chart techniques in presenting to teen-agers the "why and how" of good food habits. Its interest encompasses their parents as well as their teachers. Especially appropriate for science and health classes.

UNCLE JIM'S DAIRY FARM—non-technical—16 mm. sound—Kodachrome—11 minutes

Suitable for primary and lower levels of intermediate grades. The film shows wholesome daily living on a dairy farm. It has been designed to help build ideals of healthy, happy living and emphasizes growth as a result of healthful living.

WEIGHT REDUCTION THROUGH DIET—16 mm. sound—Kodachrome—15 1/2 minutes.

Suitable for adult and professional use. The film documents a weight reduction study at Michigan State College under the direction of Dr. Margaret A. Ohlson, Head of the Foods and Nutrition Dept.

The above four films were produced by the National Dairy Council and are available for loan from: Association Films, Inc., Broad and Elm, Ridgefield, N. J.; 351 Turk St., San Francisco 2, Calif.; 561 Hillgrove Ave., La Grange, Ill.; 1108 Jackson St., Dallas 2, Texas. (There is a postage charge)

THE STORY OF OATS AND OATMEAL—16 mm. color and sound—25 1/2 minutes.

This film highlights the growth of a plant from seed to maturity. Time-lapse photography is utilized to unfold months of plant growth in seconds. The camera records crossbreeding technics used to develop the best oat strains. Dr. Frederick J. Stare, head of the Department of Nutrition, School of Public Health of Harvard University, explains the food value found in oats. The film ends with a trip through the plant of a manufacturer of oatmeal.

Film made by John Ott Pictures, Inc. for the Quaker Oats Co. It is available from the Modern Talking Picture Service, Inc., 45 Rockefeller Plaza, New York 20, N. Y.

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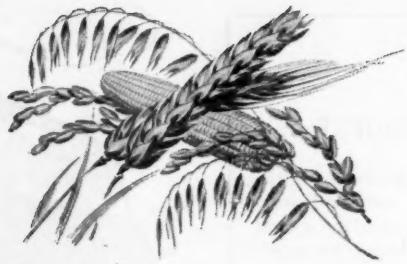

You can have a Balanced Low-Fat Breakfast!

Recently scientific and medical authorities have stated that there will probably be a trend in this country to less rich diets which means less calories in the diet. Because fats are such a concentrated source of calories, a moderate reduction of fat intake will result in a generous reduction of calories.

Medical and nutrition authorities when recommending that the fat intake of the diet be lowered state that a low-fat breakfast should provide well-balanced nourishment. *A basic cereal breakfast pattern shown below has found wide endorsement because it makes a worth-while contribution of complete protein, essential B vitamins, and minerals to the daily diet and is low in fat.*

Basic Cereal Low-Fat Breakfast Pattern

Orange juice, fresh, ½ cup, Cereal, dry weight, 1 oz., with whole milk, ½ cup, and sugar, 1 tsp., Bread, white, 2 slices, with butter, 1 tsp., Milk, nonfat (skim), 1 cup, black coffee.

Nutritive Value of Basic Cereal Breakfast Pattern

Calories	**502**
Protein	**20.5 gm.**
Fat	**11.6 gm.**
Carbohydrate	**80.7 gm.**
Calcium	**0.532 gm.**
Iron	**2.7 mg.**
Vitamin A	**600 I. U.**
Thiamine	**0.46 mg.**
Riboflavin	**0.80 mg.**
Niacin	**3.0 mg.**
Ascorbic Acid	**65.5 mg.**
Cholesterol	**32.9 mg.**

Note: **To further reduce fat and cholesterol use skim milk on cereal which reduces Fat Total to 7.0 gm. and Cholesterol Total to 16.8 mg. Preserves or honey as spread further reduces Fat and Cholesterol.**

Bowes, A. deP., and Church, C. F.: Food Values of Portions Commonly Used. 8th ed. Philadelphia: A. deP. Bowes, 1956.
Cereal Institute, Inc.: The Nutritional Contribution of Breakfast Cereals. Chicago: Cereal Institute, Inc., 1956.
Hayes, O. B., and Rose, G. K.: Supplementary Food Composition Table. J. Am. Dietet. A. 33:26, 1957.

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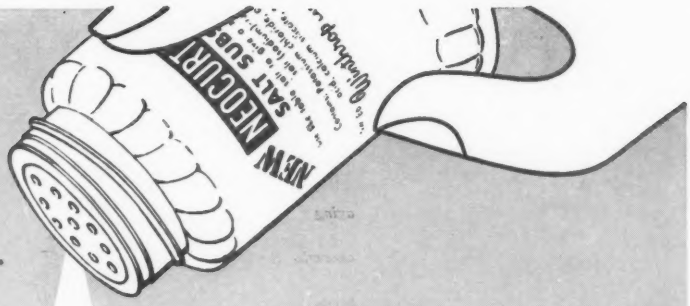

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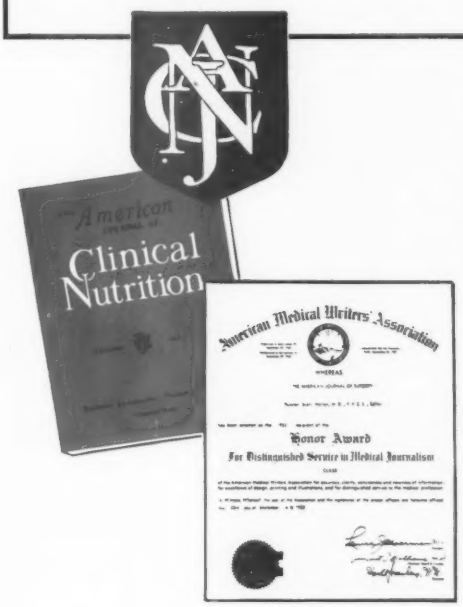

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L-Lysine Monohydrochloride	790 mg.*
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Thiamine Mononitrate	10 mg.
Riboflavin	10 mg.
Pyridoxine Hydrochloride	2 mg.
Niacinamide	100 mg.
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Carbohydrate	28.6 gm.	24.7 gm.
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*Eggnog nutritive value from Bowes & Church, 7th Ed. 1951

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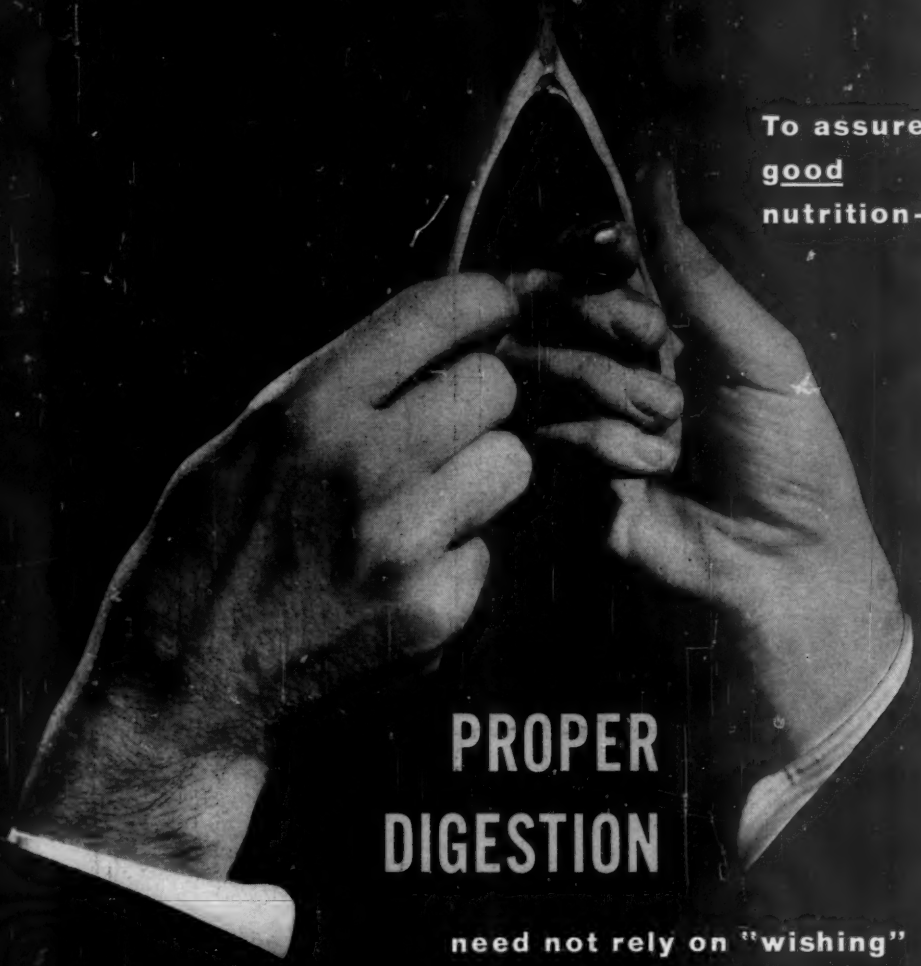

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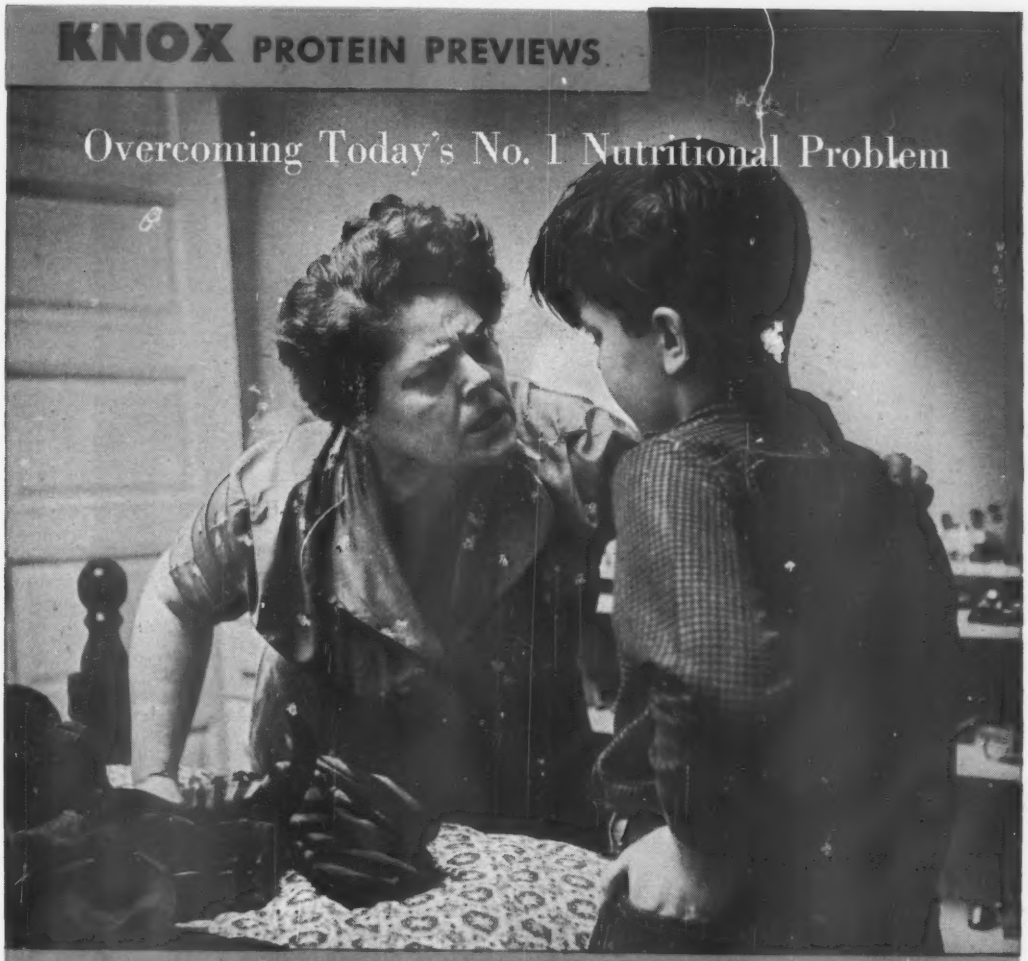

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The older man in industry needs the help of doctor, management, and homemaker . . . to extend his years of productivity.

A recent study of presumably healthy men in business showed nearly one-third to be obese. Many suffered from diseases of nutritional origin or requiring special dietary treatment.

Obesity is associated with increased incidence of many serious diseases . . . chronic illnesses occurring with about twice the frequency among obese individuals 40 to 59 years of age as among those of normal weight. At all ages, more deaths occur among the obese. Evidence indicates obesity is becoming more frequent among men . . . increasing the health hazard during middle years.

Mechanization of industry increases the value of the skilled and experienced worker . . . while decreasing his physical activity and energy needs . . . and increasing his need for choosing foods of high nutrient content in relation to calorie value. Milk is such a food.

Three glasses of milk a day . . . to drink . . . used in food preparation . . . as cheese or ice cream . . . will provide all the calcium needs of men . . . and supply generous amounts of high quality protein and other essential nutrients.

In planning meals to maintain and extend productivity of the man in industry, *milk and milk products are foundation foods for good eating and good health.*

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

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What is a Sensible Breakfast?

The division of his day into periods for productive work, for play, and for sleep makes man fare best when his total daily food intake is distributed over three sensibly organized meals.

Since a high percentage of adolescents and adults forego or skimp breakfast, the physician might well point out the need for a sensible breakfast: a meal which provides energy for a morning of productive work, which allays hunger until the noon meal, which supplies an adequate share of the day's nutrient requirements, and which consists of inviting, easily digested foods.

A dish of oatmeal helps fulfill the requirements of such a breakfast: It provides readily available energy; it helps to allay hunger throughout the morning; it makes a notable contribution to the day's nutritional needs; it fits into virtually every breakfast, including most of those especially low in calories.*

Oatmeal is richer in protein than other whole-grain breakfast cereals. None are as high in thiamine as oatmeal. Also, oatmeal provides other B-complex vitamins. Its mineral content, especially of iron and phosphorus, rates it among the leaders.

Its delicious taste and easy digestibility further qualify oatmeal as an ideal "habit food" for a sensible breakfast.

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1400 CALORIES OR LESS PER DAY	2400 CALORIES PER DAY	3000 CALORIES OR MORE PER DAY
Breakfast	**Breakfast**	**Breakfast**
Approximately 300 Calories	**Approximately 500 Calories**	**Approximately 700 Calories**
Orange juice, 4 oz.	Orange juice, 4 oz.	Orange juice, 4 oz.
Oatmeal, 1 oz. Skim milk, 4 oz. Sugar, 1 tsp.	Oatmeal, 1 oz. Milk, 4 oz. Sugar, 1 tsp.	Oatmeal, 1 oz. Milk, 4 oz. Sugar, 1 tsp.
Toast, 1 slice lightly buttered	One egg	Two eggs
†Coffee without cream or sugar	Toast, 2 slices with butter or jelly	Bacon, 2 strips
	†Coffee with cream and sugar	Toast, 2 slices with butter or jelly
		†Coffee with cream and sugar

†For children substitute 4 oz. skim milk

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For Speedy Return To Normal Nutrition

Meat...

in the congestive phase of cardiac disease

Meat fits well into the moderate-protein, restricted-sodium, acid-ash diet currently recommended for many patients with congestive cardiac failure.[1]

The protein of meat—in the proportionate arrangement of its essential amino acids—closely approaches the quantitative proportions needed to promote human tissue synthesis and repair. For this reason lean meat proves important in maintaining positive nitrogen balance without excessive protein intake.

The sodium content of meat prepared without added salt is relatively low. Per 100 grams, beef muscle meat shows approximately 50 mg. of sodium, lamb 90 mg., pork 60 mg., and veal 50 mg.[2]

The acid ash of meat aids in the promotion of diuresis.

The easy digestibility of meat is a prime requisite of foods specified for the patient with congestive cardiac disease.

In addition to these important features, meat contributes other nutritional factors essential in any convalescence —the B vitamins thiamine, riboflavin, niacin, pantothenic acid, B_6, and B_{12}, and the minerals iron, phosphorus, potassium, and magnesium.

1. Odell, W. M.: Nutrition in Cardiovascular Disease, in Wohl, M. C., and Goodhart, R. S.: Modern Nutrition in Health and Disease, Philadelphia, Lea & Febiger, 1955, p. 699.
2. Bills, C. E.; McDonald, F. G.; Niedermeier, W., and Schwartz, M. C.: Sodium and Potassium in Foods and Waters, J. Am. Dietet. A. *25*:304 (Apr.) 1949.

The nutritional statements made in this advertisement have been reviewed by the Council on Foods and Nutrition of the American Medical Association and found consistent with current authoritative medical opinion.

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ALMOST every physician makes use of nutritional principles and practice in his daily work. This is the point of view underlying The American Journal of Clinical Nutrition which conceives of nutrition as an adjunct in the total care of every patient. Cutting across arbitrary boundaries of specialties, nutrition is used by internist, surgeon, pediatrician and obstetrician alike. It has been called "the cornerstone of preventive medicine, the handmaiden of curative medicine, and the responsibility of every physician."

As part of our objective of integrating modern concepts of nutrition into clinical practice, The American Journal of Clinical Nutrition features a series of authoritative articles in the field of diet therapy. Written by eminently qualified experts in the field these concise, up-to-date reviews are prepared for the clinician in practice. The series has attracted considerable interest and in order to make this conveniently available for reference and use the publishers have decided to reprint it in a combined form. This seminar on practical nutrition presents a point of view rarely found in traditional textbooks or monographs. A glance at the wide gamut of topics listed in the table of contents will clearly illustrate the point previously made—that nutrition is part and parcel of all therapy. This anthology is presented, therefore, as a guide to better practice which is, after all, the goal of all medical workers.

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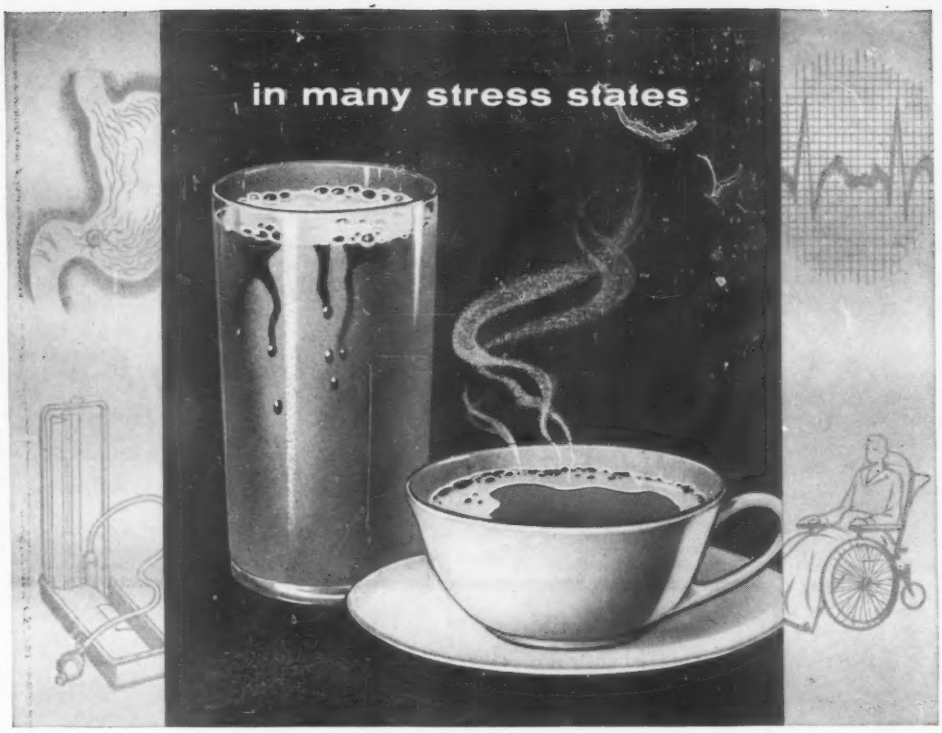

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why California table wine in the low-sodium diet?

TABLE I[1]

	No. specimens examined	Sodium (mg./100 cc.) Mean
Musts (crushed white grapes)	9	1.63
California Red Table Wines	82	5.56
California White Table Wines	73	5.44
California Dessert Wines	104	7.10

*D*ietary restriction of sodium has become a standard procedure in the control of edema associated with cirrhosis of the liver, congestive heart failure, certain kidney ailments, toxemias of pregnancy, during digitalization and in drug-induced diuresis.

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May we send you a copy of "Uses of Wine in Medical Practice"? A copy is available to you, at no expense, by writing to: Wine Advisory Board, 717 Market Street, San Francisco 3, California.

1. Lucia, S. P. and Hunt, M. L.: Am. J. Digest. Dis. 2:26 (Jan.) 1957.
2. Goetzl, F. R.: Permanente Found. M. Bull. 8:72 (April) 1950.
3. Irvin, D. L. and Goetzl, F. R.: Permanente Found. M. Bull. 9:119 (Oct.) 1951.
4. Irvin, D. L.; Durra A., and Goetzl, F. R.: Am. J. Digest. Dis. 20:117 (Jan.) 1953.

CHARTS

FREE UPON REQUEST

The following list of diet charts which are available from advertisers has been compiled from various sources. Interested readers should write to the addresses listed below for additional information—Ed.

Low Residue Diet Charts
Low Sodium Diet Charts—2000 calories
Low Sodium Diet Charts—1000 calories (reducing diet)
The Dietene Co.,
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The Dietene Co.,
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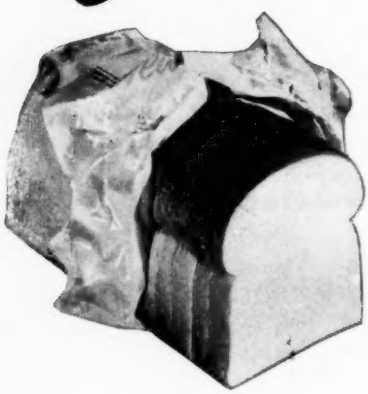

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